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Research Article

The influence of information provided prior to switching from Humira to biosimilar adalimumab on UK patients' satisfaction: a cross sectional survey by patient organisations.

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Abstract

Objectives: To investigate the perceptions and experiences of people with specific immune mediated inflammatory diseases during the process of switching from Humira to biosimilar adalimumab.

Design: Cross sectional survey

Setting: An anonymized, self-administered, web-based survey

Participants: The participants were drawn from members and non-members of either the National Rheumatoid Arthritis Society (NRAS), the National Axial Spondyloarthritis Society (NASS), Crohn's & Colitis UK (CCUK), or Psoriasis Association. Birdshot Uveitis Society and Olivia's Vision also signposted to the survey links.

Results: A total of 899 people living with various immune mediated inflammatory diseases participated in this survey. Thirty-four percent of respondents reported poor overall satisfaction with their biosimilar adalimumab after the switch, associated with complaints related to the switching process including lack of shared decision making, scarcity of information provided by or signposted to by the department instigating the switch as well as lack of training with the new injection device. Where training with the new device had been provided, there were significantly reduced reports of pain when

injecting the new biosimilar (odds ratio 0.20, 95% confidence interval 0.07 to 0.55), side effects (0.17, 0.06 to 0.47) and difficulty in using the new injection device (0.25, 0.15 to 0.41). Self-reported side effects by were reduced by 0.13, 0.05 to 0.38 when written information was provided by healthcare professionals and by 0.15, 0.05 to 0.42 with provision of verbal information. Difficulty in using the new injection device was also reduced by provision of satisfactory information written documents (0.38, 0.23 to 0.63) or by verbal communication with healthcare professionals (0.45, 0.27 to 0.73). Finally, provision of satisfactory written or verbal information was associated with a reduction in any negative perception regarding symptom control with the new biosimilar by 0.05, 0.004 to 0.57 and by 0.15, 0.03 to 0.84 respectively.

Conclusions: Patient reported experiences of the process of switching from originator to biosimilar emphasise the importance of clear communication, training and information in order to optimise perception and maximize achievable outcomes with the new treatment.

Strengths and limitations of this study

- This patient survey of 899 subjects with an immune mediated inflammatory disease indicated that paucity of information provided during the switching process from anti-TNF originator to biosimilar was associated with reduced overall satisfaction with the biosimilar.
- Provision of training with the new biosimilar device significantly reduced reports of injection pain and difficulty in device use.
- Provision of written material and verbal instruction regarding the new biosimilar device significantly reduced reports difficulty in device use.
- The study design included an open invitation to participate in the survey which may have had the limitation of introducing selection bias among respondents.
- Another limitation of the survey is that it was not designed or powered to assess any influence of the biologic formulation on the switching experience.

Introduction

Over the last two decades, biologic tumor necrosis factor (TNF) inhibitors such as adalimumab (ADA) have transformed achievable outcomes for patients with a wide variety of immune mediated inflammatory diseases including rheumatoid arthritis (RA), axial spondyloarthropathies (AS), skin psoriasis and psoriatic arthritis (PsA), Crohn's disease (CD) and other inflammatory bowel diseases such as ulcerative colitis (UC). However, the very high acquisition costs have resulted in varying degrees of restricted access across global healthcare economies. In 2017/2018, adalimumab cost the NHS in England £462m, of which £436m was spent on the drug's use in hospitals. In Scotland, the spend was in excess of £40m per annum, and in Wales, adalimumab cost secondary care £15m in 2016/2017. When originator drugs approached patent expiry, biosimilar drugs emerged, and several have been approved for use in Europe. The first to be approved were infliximab and etanercept biosimilars, and more recently adalimumab biosimilars. A commissioning framework for use of best value biological medicines (including biosimilar medicines) was published by NHS England in September 2017, setting out NHS England's position and providing a framework to help commissioners develop plans for rapid and effective uptake of the best value biological medicines[1]. In September 2018, NHS England published their commissioning intentions for

adalimumab following the loss of patent exclusivity for Humira[2]. Guidance was issued to NHS Trusts and clinical commissioning groups (CCGs) with instructions that nine out of 10 new patients should be started on the best value biologic medicine within three months of a biosimilar launch and that at least 80% of existing patients should be switched or remain on the best value biologic (which could be the originator or a biosimilar) within 12 months. These directives came with the expectation of at least £150 million savings per year by 2021. The National Rheumatoid Arthritis Society (NRAS), National Axial Spondyloarthritis Society (NASS), Crohn's & Colitis UK (CCUK), and the Psoriasis Association together welcomed the news. In a joint statement, they said: "We welcome increased availability of effective treatment options for patients and understand the importance of the wise and careful use of NHS resources. The introduction of biosimilars for adalimumab brings opportunities for both patients and the NHS. However, it is vital that patients are fully informed about all the treatment options available to them and commissioners and health professionals adopt the principles of shared decision-making."

Although some previous studies have investigated the knowledge and perception of biosimilars among patients who had not yet switched to biosimilars from originators[3 4], the satisfaction and perception of the switching process among patients who have

already experienced it remains unclear. For people living with an immune mediated inflammatory disease whose disease has been well-controlled on a biologic anti-TNF originator, having to switch to an alternative agent may cause anxiety and even suspicion, especially if it is known that the reason for switching is to save money. Therefore, it might be anticipated that provision of appropriate reassurance and relevant information during the switching process will have a substantial influence on achieving optimum outcomes and benefits.

In the present manuscript, we report the findings of a web-based survey designed by four UK patient organisations for people living with immune mediated inflammatory diseases for which biologic TNF inhibitors may be indicated, NRAS, NASS, Crohn's & Colitis UK and the Psoriasis Association UK. The survey was conducted in the UK to investigate the perceptions and experiences of patients during the process of switching from Humira to biosimilar adalimumab.

Methods

Study design, setting and population

This was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations; NRAS, NASS, Crohn's & Colitis UK or Psoriasis Association UK. In addition, the Birdshot Uveitis Society and Olivia's Vision

also signposted to the survey links. The online survey was promoted via social media platforms, online communities and through the organisations' membership communications platforms. The patients were asked to complete the survey once they had completed the switching processes. People who lived outside the UK or were aged under 18 were excluded. This survey was designed by the four patient organisations and then distributed between April 4th and November 30th 2019. The survey front page included information describing the survey and asked participants for voluntary participation. An electronic consent of voluntary participation was sought from the respondents by clicking an "agree" button. All the responders were able to review and change their responses by scrolling up and down the page before submission. Cookies were used by the survey tool to minimize the chance of more than one response per computer.

A questionnaire comprising 27 questions was hosted on an electronic survey platform (Survey Monkey) and divided into three parts in the following manner: (1) characteristics of participants (questions 1-9, 26, 27), (2) individual experience of the switching process and perception of the new biosimilar (questions 10-23) , (3) individual opinion related to the switching process (questions 24, 25), (see survey questions in Supplementary Material). Most questions were formulated as closed, multiple-choice

questions (MCQ), combined with free comments, with the exception of questions 13, 24, 25 which were full open questions. The questionnaire did not ask for any personal identifying information. All the survey questions were developed to explore individual participants' perceptions and satisfaction with the switching process from adalimumab originator to a biosimilar product. To explore the factors identified by the survey respondents which contributed to their perceptions of the switching process, we grouped them based on the level of satisfaction with the services provided by their healthcare providers before switching, such as written information, verbal information and training for the new devices. Participants answering "4 (somewhat satisfied)" or "5 (very satisfied)" in question 12 were assigned to a category designated as "satisfied" and those responding that they were "1 (not at all satisfied)" or "2 (somewhat dissatisfied)" were assigned to a category of "dissatisfied". Participants responding as "3 (neither)" or "not applicable (N/A)" were excluded from these categories. With respect to the participants' perceptions of efficacy of the biosimilar, patients who answered "slightly better" and "much better" in question 15 to 18 were assigned to a category of "better perception" and those who answered "slightly worse" and "much worse" were assigned to a category of "worse perception". Those participants responding that the efficacy of the biosimilar was "the same" as originator or "not applicable (N/A)" were excluded from these categories.

Patient and Public Involvement

The survey questions were designed by members of the four national patient organisations and the survey itself was hosted on the websites of each of the four patient organisations. Members of the organisations and non-members visiting the website were invited to participate in the survey. Members of the four organisations made data available to the corresponding author, who is chief medical advisor to NRAS, and his colleagues for analysis. Members of the patient organisations have commented on the findings, contributed to writing and have approved the final version of this manuscript.

Statistical analyses

The survey responses to the closed questions formulated as MCQs were collected and presented as number and percentages of responding patients. Variables were based on the choices of MCQ options. Disease activity was self-reported by the participants in question 9. Comparison of frequency of responses which showed “better” or “worse perception” between “the satisfied group” and “the dissatisfied group” were expressed as Odds ratios (OR) and 95% confidential intervals (95%CI). *P* values were assigned based on the chi-square test for categorical values when their expected values were higher than 10 and Fisher’s exact test was conducted if expected values of categorical values were smaller than with 10. *P* values less than 0.05 was considered statistically

significant. A multiple categorical logistic regression analysis was used to select factors significantly associated with a positive perception of the new biosimilars following the switching process, after adjusting for gender, self-reported disease activity and biosimilar brands. All analyses were performed in JMP version 14.0 for windows.

Results

Participants

A total of 899 patients with different immune mediated inflammatory diseases participated in this survey. The largest response came from patients with Crohn's Disease (42%) followed by RA/JIA (25%), AS (19%) and skin psoriasis and PsA (13%). Most of the participants (52%) had been taking Humira® for between one to five years; about one fifth were recent users (<1y) and almost one fifth were long-term users (>5y). By self-evaluation of disease activity, the majority (62%) were very well controlled, and 26% well controlled. Ten percent of participants had undertaken the survey just after their first injection of the new biosimilar. (Table 1).

The patients' experience and satisfaction with experience of switching process

Concerns about switching had been shared with the healthcare team by 43% of respondents and about a third of these (16 % of all survey participants) did not have their concerns satisfactorily dealt with. Over half of respondents (53%) reported not being

asked for consent before switching and the majority of respondents reported poor overall satisfaction with their biosimilar adalimumab after the switch with only 8% “very satisfied”, while 34% were “not at all satisfied” (Table 2).

Sixteen percent of participants were not at all satisfied with the written information about the switch to a biosimilar and 23% were dissatisfied with the verbal information received from their healthcare professionals. The lack of training with the new injection device was also highlighted by 21% of respondents. Furthermore, more than half reported that they were not given an option to decline the switch or to delay it (56% and 52%, respectively) (Figure 1).

After switching from originator to biosimilar, the most commonly reported problem was that of “worse pain” on injection with the biosimilar compared to originator. The injection pain was said to be “much worse” by 51% and “slightly worse” by 23% (Figure 1.). Ease of using the injection device was reported to be much worse by 22% of respondents. With respect to symptom control after the switch, 47% reported it to be the same or better (2%) than with originator. However, 20% reported that their symptoms were “much worse” (Figure 1). Respondents rating themselves as having higher disease activity tended to report greater dissatisfaction with all aspects of the switching process including written information, verbal information and training on the new injection devices (Table S1).

Comparison of proportion of patients with worse perception or better perception of the new biosimilars between those expressing satisfaction and dissatisfaction in the switching process

The proportion of participants with worse perception of the new biosimilar in term of side effects, ease of using the injection device and managing their symptoms was lower in the patients satisfied with the written and verbal information. Aside from that, respondents satisfied with the training for the new injection device reported fewer side effects, less pain when injecting and reduced difficulty in use of the injection device after the switching process (all *P* values are than 0.05) (Table S2).

The benefits of informative communication and training in use of a new injection device on patients' perception of a new biosimilar

Results of the final logistic regression model incorporating gender, self-reported disease activity and biosimilar brand are summarized in Figure 2. The training in use of the new injection device was associated with a significant reduction in reported pain on administering the new biosimilar (OR[95% CI]: 0.20, 0.07 to 0.55), reporting of side effects (0.17, 0.06 to 0.47) and difficulty in using the device (0.25, 0.15 to 0.41). Both satisfaction with written and verbal information about the switch to biosimilar provided by healthcare professionals was associated with fewer reported side effects (0.13, 0.05 to

0.38 in respect of the written information and 0.15, 0.05 to 0.42 in respect of the verbal information). Furthermore, provision of information perceived as being satisfactory significantly reduced participants' complaints regarding use of the new biosimilar injection device (0.38, 0.23 to 0.63 in respect of the written information and 0.45, 0.27 to 0.73 in respect of the verbal information) as well as in managing their self-reported disease activity as compared with originator adalimumab (0.05, 0.004 to 0.57 and 0.15, 0.03 to 0.84 respectively).

Discussion

Biologic drugs comprise peptides or proteins that are produced in living cells. Monoclonal antibodies are particularly large and complex proteins. Even when the primary amino acid sequences are identical, as in the case of originator and biosimilar biologics, there may be differences in quaternary structure and post-translational modifications. However, in order to be designated a biosimilar, a biologic has to demonstrate very vigorous similarities to the originator in terms of a wide range of parameters including antigen binding and antibody function as well as providing clinical trial data that demonstrates equivalent efficacy in an indication for which the originator has been approved[5-10].

By means of a truncated clinical trial development program, reduced research and development costs, and economic competition, approved biosimilars reach the

marketplace with favourable health economic benefits with an expectation of equivalent clinical efficacy at a cohort level. From the perspective of healthcare economies, the potential savings generated by switching from originator to biosimilar products become very attractive. For some healthcare systems for which biologics are purchased on the basis of a national or regional tender, such as Norway[11 12] or UK, for example, the originator drug price can also be lowered and compete in the tender process. While this is very attractive for payers, it may appear much less so for patients who have responded well to an originator. They may initially be suspicious that they are being provided with a cheaper, and possibly less effective biologic alternative, purely to save money. While the complexity of clinical and biochemical evidence to support therapeutic equivalence between biosimilar and originator has been established prior to approval of a biosimilar, this is unlikely to be known to the lay public and patients without a comprehensible explanation. And even then, there may be differences in biologic formulation as there were in the case of this switch from Humira to adalimumab, such as citrated versus non citrated, and the injection device itself, which might give rise to differences in individual experiences of the tolerability and ease of use between an originator or biosimilar. Of note, 22% of respondents reported the ease of using the injection device to be much worse following the switch to biosimilar. Such practical difficulties may have deleterious

consequences for medication adherence, either intentionally or non-intentionally. Ideally, it is important for a patient to be able to familiarize themselves with the new biosimilar delivery device prior to any switch in biologic medication and to have the option to switch to a different device[13].

What is striking about this important survey, designed and initiated by the patient organisations, is that it illustrates the importance of good, clear and constructive communication around the switching process if patients are to achieve the best outcomes. The survey findings also suggest that with respect to switching from adalimumab originator to biosimilar, that this was often done with suboptimal communication. A limitation in the survey design and invitation to participate is in the potential for selection bias among responders, therefore the high proportion of respondents (about two thirds) expressing dissatisfaction with the switching process, may be an over-estimate of the wider population switched. Another limitation of the survey is that it was not designed or powered to assess any influence of the biologic formulation, such as citrated or non-citrated, on the switching experience. Nonetheless, our findings unequivocally highlights the importance of provision of clear, co-produced information about the switch to biosimilar as well as appropriate training in the use of a new injection device. The clear consequence of this best practice is a reduction in

reported side effects and injection related pain as well as improved ease of using the injection device and management and control of symptoms.

While so-called "nocebo" responses have been previously documented[11 14-18] , and could be augmented by poor communication around the switching process, the findings highlight the importance of healthcare professionals listening to their patients' experiences, taking them seriously and acting to investigate and resolve issues satisfactorily when they are reported. Among this large sample of survey respondents, a high proportion report receiving inadequate information at the time of switch to adalimumab biosimilar. Even when taking into consideration that there may have been selection bias among respondents, this study illustrates that specialist physicians and health care providers still have much to do in order to communicate the likelihood of maintained benefits to the individual being switched, and also the potential for widening access to expensive drugs, as well as the economic benefits for the wider health care economy in fact, many patients accept the switch to biosimilars on the false premise of altruistic thinking that more people with the same health condition be prescribed an anti-TNF. Unfortunately, this has not been possible while current NICE guidance has set the threshold of high disease activity for access to a biological anti-TNF for people with certain immune mediated inflammatory diseases, for example, RA[19], Crohn's disease[20]

and skin psoriasis[21]. A challenge for the future will be whether the biosimilars might regarded as sufficiently cost-effective to allow access for patients with moderately active disease, as is the case in many other European health economies.

As more biosimilar drugs are anticipated in the future, the learnings from this study should help inform best practice with respect to the switching process, involving good communication with the patient and meaningful shared decision making, thereby facilitating best achievable outcomes.

Table 1. Participant characteristics

Characteristics	Participants (n= 899)	
Female, n (%)	609	(68)
Age, n (%)		
18-24	76	(8)
25-44	323	(36)
45-64	375	(42)
65+	118	(13)
Medical conditions, n (%)		
Crohn's Disease and Ulcerative colitis	376	(42)
Rheumatoid arthritis and Juvenile Idiopathic Arthritis	227	(25)
Axial spondyloarthritis including ankylosing spondylitis	170	(19)
Skin psoriasis and Psoriatic arthritis	112	(13)
Others	11	(1)
Period of Humira use before switching, n (%)		
Less than 1 year	204	(23)
More than 1 year to 5 years	468	(52)
More than 5 years	227	(25)
Patient-assessed disease activity, n (%)		
Very well controlled	564	(63)
controlled well	225	(25)
Neither	85	(9)
Not controlled	12	(1)
Not controlled well at all	10	(1)
Number of the new biosimilar injections before survey, n (%)		
1	92	(10)
2 to 4	318	(36)
5 to 10	372	(42)
More than 10	110	(12)
Biosimilar, n (%)		
Imraldi®	561	(62)
Amgevita®	237	(26)
Hyrimoz®	56	(6)

Valuables presented as n (%)

Table 2. Patient's experience in the process of switching

Questions	Answers	Participants (n=899)	
		n	(%)
1. Have you shared any concerns you may have with your consultant, specialist nurse, pharmacist, or GP?	Yes	388	(43)
	No	423	(47)
	I didn't know I could	87	(10)
2. Do you feel they have they offered you a satisfactory solution? ‡	Yes, I was offered a switch back to my original treatment	65	(7)
	Yes, I was offered a switch to another treatment	41	(5)
	No	139	(16)
3. Did your consultant, specialist nurse or pharmacist seek your consent to switch from Humira to a biosimilar?	Yes	359	(40)
	No	477	(53)
	Not sure / can't remember	63	(7)
4. Overall, how satisfied are you with your new biosimilar? †	Very satisfied	74	(8)
	Satisfied	177	(20)
	Neither	132	(15)
	Somewhat satisfied	202	(23)
	Not at all satisfied	307	(34)

‡The patients who have answered "yes" in Question 1(n=388) have proceeded to Question 2. †Seven answers were missing in Question4.

Summary box

Section 1: What is already known on this topic

The very high acquisition costs of biologic TNF inhibitors such as Humira have resulted in restricted access across global healthcare economies.

In 2018, NHS England published their intentions with instructions that at least 80% of patients who use Humira should be switched to the best value biosimilar within 12 months.

The patient organisations welcomed NHS's policy, but they required that patients should be fully informed about the treatment options and health professionals adopt the principles of shared decision-making.

Section 2: What this study adds

Participants who responded to the survey request by the patient organisations reported poor satisfaction with the switching process to biosimilar due to paucity of information and training.

Where good information and training were provided, it was associated with reduction in self-reported side effects and injection related pain as well as greater ease of use of the injection device and management and control of symptoms.

Authors Contributions: PCT assumes overall responsibility for the work and all the reported data. CJ, AB, SD, SB, HA designed the patient survey and were involved in data collection. PCT and KK wrote the first draft of the manuscript. KK, DP-A and PCT analysed the data. All authors contributed to discussion and interpretation of the results, critically reviewed the manuscript and approved the final version to be submitted.

Transparency: PCT affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; there have been no discrepancies from the study as planned

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Ethical approval: Not required.

Data sharing: Raw anonymous data is available to researchers on application to the

patient organisations involved who will jointly assess any applications.

Dissemination Statement: The results will be shared with the study participants and the contributing patient organisations.

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third party to do any or all of the above.

Figure legends.

Figure 1.

Donut charts illustrating the percentage of patients expressing different levels of satisfaction with various experiences associated with the switching process.

Figure 2.

Adjusted odds rations illustrating the influence of training and information from healthcare professionals in improving perception of the new biosimilar. Adjusted odds ratio and 95% confidential intervals were calculated by a multiple categorical logistic regression analysis using gender, self-reported disease activity and biosimilar brands as adjusted variables. Data to the left of the adjusted odds ratio of 1 indicates a more favourable perception.

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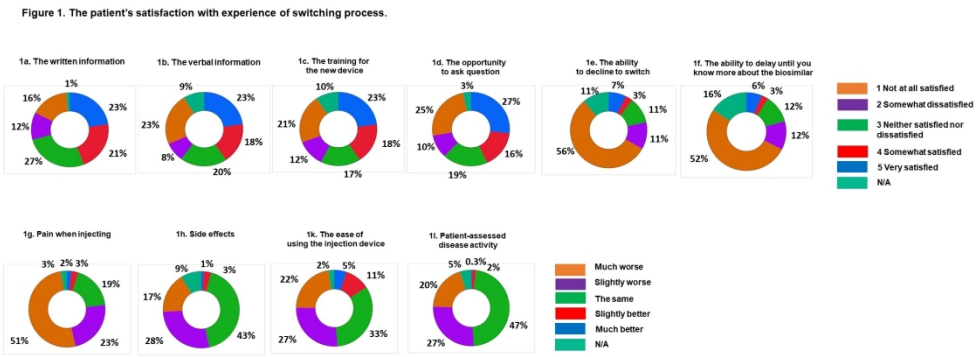

Figure 1. Donut charts illustrating the percentage of patients expressing different levels of satisfaction with various experiences associated with the switching process.

602x338mm (96 x 96 DPI)

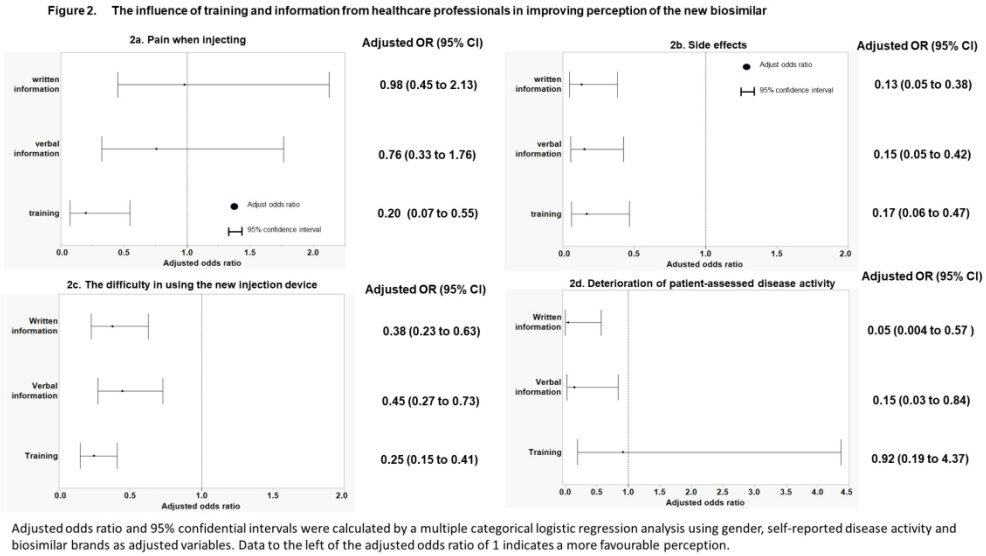

Figure 2. Adjusted odds rations illustrating the influence of training and information from healthcare professionals in improving perception of the new biosimilar. Adjusted odds ratio and 95% confidential intervals were calculated by a multiple categorical logistic regression analysis using gender, self-reported disease activity and biosimilar brands as adjusted variables. Data to the left of the adjusted odds ratio of 1 indicates a more favourable perception.

602x338mm (96 x 96 DPI)

TableS1. Comparison of characteristics of the participants between satisfied group and dissatisfied group with each experience in switching process.

Characteristics	The written information					The verbal information					The training for the new device				
	Satisfied group (N=394)		Dissatisfied group (N=249)		*p value*	Satisfied group (N=362)		Dissatisfied group (N=277)		*p value*	Satisfied group (N=364)		Dissatisfied group (N=295)		*p value*
Gender, n (%)					0.5201					0.3189					**0.00458***
Female	258	(66)	170	(69)		235	(65)	192	(70)		235	(65)	214	(74)	
Male	130	(33)	75	(30)		121	(34)	82	(30)		125	(34)	74	(26)	
Prefer not to say	4	(1)	1	(0)		4	(1)	1	(0)		3	(1)	2	(1)	
Age, n (%)					0.0546					**0.0003***					0.1091
18-24	28	(7)	24	(10)		25	(7)	27	(10)		26	(7)	26	(9)	
25-34	56	(14)	52	(21)		51	(14)	61	(22)		57	(16)	65	(22)	
35-44	70	(18)	50	(20)		55	(15)	59	(21)		71	(20)	62	(21)	
45-54	94	(24)	58	(23)		85	(23)	66	(24)		74	(20)	61	(21)	
55-64	80	(20)	40	(16)		78	(22)	38	(14)		77	(21)	45	(15)	
65+	61	(15)	24	(10)		63	(17)	25	(9)		54	(15)	35	(12)	
Prefer not to say	5	(1)	1	(0)		5	(1)	1	(0)		5	(1)	1	(0)	
Living areas, n (%)					0.3173					**0.0267***					0.9099
South East	101	(26)	69	(28)		96	(27)	72	(26)		95	(26)	80	(27)	
South West	75	(19)	43	(17)		76	(21)	48	(17)		68	(19)	60	(20)	
North East and Yorkshire	52	(13)	27	(11)		53	(15)	28	(10)		49	(13)	34	(12)	
Midlands	42	(11)	41	(16)		31	(9)	51	(18)		46	(13)	33	(11)	
East of England	46	(12)	17	(7)		37	(10)	28	(10)		39	(11)	28	(9)	
North West	31	(8)	17	(7)		26	(7)	18	(7)		28	(8)	19	(6)	
London	22	(6)	20	(8)		19	(5)	22	(8)		21	(6)	24	(8)	
Scotland	16	(4)	6	(2)		14	(4)	4	(1)		8	(2)	11	(4)	
Wales	6	(2)	6	(2)		7	(2)	4	(1)		6	(2)	4	(1)	

Northern Ireland	1	(0)	1	(0)		1	(0)	1	(0)		2	(1)	1	(0)	
Channel Islands	1	(0)	1	(0)		1	(0)	0	(0)		1	(0)	0	(0)	
Isle of Wight	1	(0)	1	(0)		1	(0)	1	(0)		1	(0)	1	(0)	
Medical conditions, n (%)					0.2988					0.0587					0.1358
CD	144	(37)	74	(30)		122	(34)	93	(34)		125	(35)	104	(35)	
RA/JIA	104	(27)	64	(26)		106	(29)	54	(19)		94	(26)	69	(23)	
AS	79	(20)	53	(21)		70	(19)	60	(22)		82	(23)	49	(17)	
PsA	22	(6)	24	(10)		23	(6)	30	(11)		22	(6)	30	(10)	
UC	25	(6)	19	(8)		23	(6)	26	(9)		21	(6)	24	(8)	
Psoriasis	15	(4)	11	(4)		13	(4)	11	(4)		14	(4)	12	(4)	
Others	3	(1)	4	(2)		4	(1)	3	(1)		4	(1)	7	(2)	
Period of Humira use before switching, n (%)					0.1228					**0.0095***					0.3304
3 months or less	14	(4)	14	(6)		12	(3)	11	(4)		14	(4)	16	(5)	
More than 3 months to 1 year	66	(17)	51	(20)		60	(17)	53	(19)		61	(17)	58	(20)	
More than 1 year to 5 years	208	(53)	130	(52)		177	(49)	159	(57)		188	(52)	152	(52)	
More than 5 years to 10 years	68	(17)	42	(17)		72	(20)	41	(15)		68	(19)	53	(18)	
More than 10 years	38	(10)	12	(5)		41	(11)	13	(5)		33	(9)	16	(5)	
Self-reported disease activity, n (%)					**0.0282***					**0.041***					**0.0358***
Very well controlled	243	(62)	157	(63)		229	(63)	174	(63)		226	(62)	190	(65)	
controlled well	104	(26)	64	(26)		99	(27)	69	(25)		84	(23)	80	(27)	
Neither	40	(10)	21	(8)		26	(7)	25	(9)		42	(12)	18	(6)	
Not controlled	1	(0)	6	(2)		2	(1)	7	(3)		4	(1)	5	(2)	
Not controlled well at all	6	(2)	0	(0)		6	(2)	0	(0)		7	(2)	1	(0)	

No. of injections of the new biosimilar before survey, n (%)					0.3279					0.4633				0.1015
1	35	(9)	27	(11)		32	(9)	29	(11)		37	(10)	31	(11)	
2	54	(14)	26	(11)		43	(12)	31	(11)		51	(14)	25	(9)	
3	55	(14)	25	(10)		49	(14)	28	(10)		48	(13)	31	(11)	
4	37	(9)	31	(13)		40	(11)	29	(11)		40	(11)	35	(12)	
5	25	(6)	26	(11)		22	(6)	21	(8)		16	(4)	30	(10)	
6	60	(15)	30	(12)		52	(14)	46	(17)		50	(14)	46	(16)	
7	18	(5)	12	(5)		15	(4)	13	(5)		13	(4)	11	(4)	
8	33	(8)	22	(9)		22	(6)	27	(10)		26	(7)	27	(9)	
9	10	(3)	8	(3)		12	(3)	9	(3)		9	(2)	8	(3)	
10	13	(3)	12	(5)		18	(5)	12	(4)		19	(5)	11	(4)	
More than 10	52	(13)	27	(11)		55	(15)	27	(10)		53	(15)	36	(12)	

CD, Crohn's Disease, RA, Rheumatoid arthritis, JIA, Juvenile Idiopathic Arthritis, AS, Axial spondyloarthritis including ankylosing spondylitis, PsA, Psoriatic arthritis, UC, Ulcerative colitis, Valuables presented as n (%), P values were assigned based on the chi-square test for categorical value when it's expected value is higher than 10 and Fisher's exact test was conducted if the expected values of categorical values were smaller than 10. *P values less than 0.05 was considered statistically significant.

Table S2a

		Comparison of proportion of patients with "worse perception" or "better perception" on the new biosimilars between those expressing satisfaction and dissatisfaction in the switching process									
		The written information									
		satisfied group (N=394)		dissatisfied group (N=249)		Neither (N=238)		N/A (N=13)		*unadjusted OR (95%CI)	*p value
Side effects	worse perception, n (%)	118	(30)	158	(63)	117	(49)	7	(54)	**0.15 (0.06-0.40)**	**<.0001†**
	better perception, n (%)	25	(6)	5	(2)	6	(3)	1	(8)		
	the same, n (%)	218	(56)	58	(23)	101	(42)	1	(8)		
	N/A, n (%)	31	(8)	28	(11)	14	(6)	4	(31)		
Pain when injecting	worse perception, n (%)	275	(70)	194	(78)	183	(77)	9	(69)	0.90 (0.45-1.81)	0.861
	better perception, n (%)	22	(6)	14	(6)	6	(3)	0	(0)		
	the same, n (%)	87	(22)	31	(13)	46	(19)	1	(8)		
	N/A, n (%)	8	(2)	9	(4)	3	(1)	3	(23)		
The ease of using the injection device	worse perception, n (%)	159	(40)	153	(62)	118	(50)	5	(38)	**0.35 (0.21-0.58)**	**<.0001†**
	better perception, n (%)	77	(20)	26	(10)	35	(15)	2	(15)		
	the same, n (%)	146	(37)	64	(26)	81	(34)	3	(23)		
	N/A, n (%)	11	(3)	5	(2)	3	(1)	3	(23)		
Managing symptoms	worse perception, n (%)	112	(28)	172	69.1	123	(52)	5	(38)	**0.11 (0.02-0.49)**	**0.0011†**
	better perception, n (%)	12	(3)	2	0.8	4	(2)	0	(0)		
	the same, n (%)	254	(64)	57	22.9	103	(44)	5	(38)		
	N/A, n (%)	16	(4)	18	7.23	6	(3)	3	(23)		

Valuables presented as n (%). *Comparison of frequency of responses with "worse perception" and "better perception" of the new biosimilar compared to originator between "satisfied group" and "dissatisfied group" with the experiences in the switching process to biosimilar were expressed as unadjusted odds ratios (OR), 95% confidential intervals (95%CI) and *p* values. Responses expressing "3 (neither)" or "not applicable (N/A)" in terms of satisfaction with the services in switching process and "the same" or "N/A" in terms of

the perception of the new biosimilar were excluded from the analysis. P values were assigned based on the chi-square test for categorical value when it's expected value is higher than 10 and Fisher's exact test was conducted if the expected values of categorical values were smaller than 10. †P values less than 0.05 was considered statistically significant.

Table S2b **Comparison of proportion of patients with "worse perception" or "better perception" on the new biosimilars between those expressing satisfaction and dissatisfaction in the switching process**

		The verbal information									
		Satisfied group (N=362)		Dissatisfied group (N=277)		Neither (N=175)		N/A (N=79)		*unadjusted OR (95%CI)	*p value
Side effects	Worse perception, n (%)	117	(33)	164	(59)	83	(47)	34	(43)	**0.15 (0.06-0.40)**	**<.0001†**
	Better perception, n (%)	24	(7)	5	(2)	5	(3)	3	(4)		
	The same, n (%)	192	(53)	79	(29)	76	(43)	31	(39)		
	N/A, n (%)	27	(8)	29	(10)	11	(6)	11	(14)		
Pain when injecting	Worse perception, n (%)	258	(71)	225	(82)	125	(72)	52	(66)	0.67 (0.30-1.50)	0.428
	Better perception, n (%)	17	(5)	10	(4)	13	(7)	3	(4)		
	The same, n (%)	76	(21)	34	(12)	34	(20)	20	(25)		
	N/A, n (%)	10	(3)	7	(3)	2	(1)	4	(5)		
The ease of using the injection device	Worse perception, n (%)	153	(42)	166	(60)	84	(48)	32	(41)	**0.45 (0.28-0.72)**	**0.0008†**
	Better perception, n (%)	66	(18)	32	(12)	26	(15)	16	(20)		
	The same, n (%)	130	(36)	73	(27)	63	(36)	27	(34)		
	N/A, n (%)	12	(3)	4	(1)	2	(1)	4	(5)		
Managing symptoms	Worse perception, n (%)	117	(32)	175	(63)	89	(51)	32	(41)	**0.20 (0.05-0.74)**	**0.0177†**
	Better perception, n (%)	10	(3)	3	(1)	(3)	(2)	2	(3)		
	The same, n (%)	221	(61)	76	(27)	(75)	(43)	45	(57)		
	N/A, n (%)	13	(4)	23	(8)	(7)	(4)	0	(0)		

Valuables presented as n (%). *Comparison of frequency of responses with "worse perception" and "better perception" of the new biosimilar compared to originator between “satisfied group” and “dissatisfied group” with the experiences in the switching process to biosimilar were expressed as unadjusted odds ratios (OR), 95% confidential intervals (95%CI) and *p* values. Responses expressing “3 (neither)” or “not applicable (N/A)“ in terms of satisfaction with the services in switching process and “the same” or “N/A” in terms of the perception of the new biosimilar were excluded from the analysis. P values were assigned based on the chi-square test for categorical value when it’s expected value is higher than 10 and Fisher’s exact test was conducted if the expected values of categorical values were smaller than 10. †P values less than 0.05 was considered statistically significant.

Table S2c

Comparison of proportion of patients with "worse perception" or "better perception" on the new biosimilars between those expressing satisfaction and dissatisfaction in the switching process

		The training									
		satisfied group (N=364)		dissatisfied group (N=295)		Neither (N=149)		N/A (N=86)		*unadjusted OR (95%CI)	*p value
Side effects	worse perception, n (%)	133	(37)	176	(60)	65	(44)	25	(29)	**0.15 (0.06-0.41)**	**<.0001†**
	better perception, n (%)	25	(7)	5	(2)	4	(3)	3	(4)		
	the same, n (%)	176	(48)	90	(31)	65	(44)	47	(55)		
	N/A, n (%)	29	(8)	24	(8)	15	(10)	10	(12)		
The ease of Pain when injecting	worse perception, n (%)	254	(70)	242	(83)	113	(76)	52	(60)	**0.19 (0.07-0.49)**	**0.0001†**
	better perception, n (%)	28	(8)	5	(2)	8	(5)	2	(2)		
	the same, n (%)	75	(21)	38	(13)	27	(18)	24	(28)		
	N/A, n (%)	6	(2)	8	(3)	1	(1)	8	(9)		
The ease of using the injection device	worse perception, n (%)	134	(37)	194	(66)	76	(51)	32	(37)	**0.24 (0.15-0.40)**	**<.0001†**
	better perception, n (%)	79	(22)	28	(10)	20	(14)	13	(15)		
	the same, n (%)	144	(40)	66	(22)	51	(34)	32	(37)		
	N/A, n (%)	6	(2)	6	(2)	1	(1)	9	(10)		
The ease of Managing symptoms	worse perception, n (%)	136	(37)	178	(60)	67	(45)	33	(38)	0.38 (0.11-1.30)	0.1412
	better perception, n (%)	8	(2)	4	(1)	4	(3)	2	(2)		
	the same, n (%)	201	(55)	97	(33)	73	(49)	46	(53)		
	N/A, n (%)	18	(5)	16	(5)	4	(3)	5	(6)		

Valuables presented as n (%). *Comparison of frequency of responses with "worse perception" and "better perception" of the new biosimilar compared to originator between "satisfied group" and "dissatisfied group" with the experiences in the switching process to biosimilar were expressed as unadjusted odds ratios (OR), 95% confidential intervals (95%CI) and *p* values. Responses expressing "3 (neither)" or "not applicable (N/A)" in terms of satisfaction with the services in switching process and "the same" or "N/A" in terms of the perception of the new biosimilar were excluded from the analysis. P values were assigned based on the chi-square test for categorical value when it's expected value is higher than 10 and Fisher's exact test was conducted if the expected values of categorical values were smaller than 10. †P values less than 0.05 was considered statistically significant.

We want to understand the recent experiences of people living in the UK who have switched from Humira to an adalimumab biosimilar medication.

If you haven't been asked to switch yet please note that we will keep this survey open for a few months so do feel that you can come back to it.

This survey is for only for people living in the UK aged 18+

1. Do you live in the UK?

○ Yes
○ No

2. What area of the UK do you live in?

○ Scotland
○ Wales
○ Northern Ireland
○ Isle of Man
○ Channel Islands
○ North East and Yorkshire
○ North West
○ Midlands
○ East of England
○ South West
○ South East
○ London

3. Were you being treated with Humira (adalimumab) during 2018?

○ Yes
○ No

4. What medical condition was your Humira primarily prescribed for?

- ○ Axial spondyloarthritis including ankylosing spondylitis (AS)
- ○ Crohn's Disease
- ○ Ulcerative colitis
- ○ Another form of IBD
- ○ Hidradenitis Suppurativa
- ○ Psoriasis
- ○ Psoriatic arthritis
- ○ Rheumatoid arthritis (RA)
- ○ Juvenile Idiopathic Arthritis (JIA)
- ○ Uveitis
- ○ Other (please specify)

5. Have you switched from Humira to an adalimumab biosimilar?

- ○ Yes
- ○ No

6. Did your consultant, specialist nurse or pharmacist seek your consent to switch from Humira to a biosimilar?

- ○ Yes
- ○ No
- ○ Not sure / can't remember

7. Which biosimilar medication have you switched to?

- ○ Amgevita
- ○ Hulio
- ○ Hyrimoz
- ○ Imraldi
- ○ Don't know/not sure

8. How long were you taking Humira prior to being switched?

- ○ 3 months or less
- ○ More than 3 months to 1 year
- ○ More than 1 year to 5 years
- ○ More than 5 years to 10 years
- ○ More than 10 years

9. Thinking about the time you were being treated with Humira (adalimumab) how well do you feel your disease was controlled? Please use the scale of 1 to 5 where 1 means your condition was not controlled well at all and 5 means very well controlled

Not at all satisfied	Somewhat dissatisfied	Neither satisfied nor dissatisfied	Somewhat satisfied	Very satisfied	N/A
○	○	○	○	○	○

Now, thinking about the process of switching

10. In which of the following ways did you first hear you may be asked to switch to a biosimilar?

- ○ I was told about the potential to switch face to face in clinic by my consultant
- ○ I was told about the potential to switch face to face in clinic by my specialist nurse
- ○ I was invited to a patient information meeting about biosimilars
- ○ I received a letter from the hospital
- ○ I received a letter from the homecare delivery company
- ○ I received a telephone call from the specialist nurse
- ○ I received a telephone call from the homecare delivery company
- ○ I received a telephone call from the hospital pharmacy
- ○ I received no prior notice of my treatment being switched
- ○ Other (please specify)

11. Thinking about what you heard about switching, which of the following information did you pick up from what you were told or given in writing?

- ○ Switching to biosimilars will save the NHS money
- ○ Biosimilars are almost identical and I should notice no difference in my symptoms or side effects
- ○ Switching to biosimilars will mean my hospital department would benefit and might be able to offer improved services to patients
- ○ Switching to biosimilars means more patients would be able to get prescribed these medications
- ○ I had a choice and could choose not to switch if I preferred
- ○ I would be switched to a biosimilar medication and there were no other options
- ○ I was given links to more information on biosimilars (e.g. on patient organisation websites)
- ○ Who to contact with any queries I may have about biosimilars
- ○ Other (please specify)

12. Thinking about your experience of the switching process, how would you rate your satisfaction with...

	Not at all satisfied	Somewhat dissatisfied	Neither satisfied nor dissatisfied	Somewhat satisfied	Very satisfied	N/A
The written information you received about the switch to a biosimilar	○	○	○	○	○	○
The verbal information you received about the switch from your healthcare professional	○	○	○	○	○	○
The opportunity to ask questions	○	○	○	○	○	○
The training for the new device	○	○	○	○	○	○
The ability to decline to switch	○	○	○	○	○	○
The ability to delay switching until you knew more about the biosimilar	○	○	○	○	○	○

13. What, if anything, do you think could have been done better to help the switching process run more smoothly?

Now, thinking about the biosimilar you were switched to

14. How many injections of the new biosimilar would you estimate you have taken so far?

- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 7
- ○ 8
- ○ 9
- ○ 10
- ○ More than 10

15. Thinking about how you feel the new biosimilar is working for you in terms of managing your symptoms compared with Humira would you say it is...

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

16. And what about in terms of side effects?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

17. And pain when injecting?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

18. And the ease of using the injection device?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

19. And the ease of accessing the injection device via the external packaging?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

20. And the Homecare company arrangements?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

21. And overall, how satisfied are you with your new biosimilar? Scale of 1 to 5 where 5 is very satisfied and 1 is not at all satisfied

Not at all satisfied	Somewhat satisfied	Neither	Satisfied	Very satisfied
○	○	○	○	○

And why do you say that?

22. And have you shared any concerns you may have with your consultant, specialist nurse, pharmacist, physiotherapist or GP?

○ Yes
○ No
○ I didn't know I could

23. And do you feel they have they offered you a satisfactory solution?

○ Yes, I was offered a switch back to my original treatment
○ Yes, I was offered a switch to another treatment
○ No
○ Other (please specify)

24. What do you think is most important for hospitals to be aware of as part of the switching process for new patients going forward?

25. Do you have any other comments about your experience of the biosimilar switching process?

Thank you for your time, can we just ask you for some information about yourself.

26. Gender

- ○ Female
- ○ Male
- ○ Other
- ○ Prefer not to say

27. Age

- ○ 18-24
- ○ 25-34
- ○ 35-44
- ○ 45-54
- ○ 55-64
- ○ 65+
- ○ Prefer not to say

If you are experiencing side effects with any medication please do remember anyone can report suspected side effects using the Yellow Card Scheme. Visit: mhra.gov.uk/yellowcard or call 0808 100 3352 for a paper form.

Do also speak to your rheumatologist or rheumatology nurse.

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The influence of information provided prior to switching from Humira to biosimilar adalimumab on UK patients' satisfaction: a cross sectional survey by patient organisations.

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Research Article

The influence of information provided prior to switching from Humira to biosimilar adalimumab on UK patients' satisfaction: a cross sectional survey by patient organisations.

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Abstract

Objectives: To investigate the perceptions and experiences of people with specific immune mediated inflammatory diseases during the process of switching from Humira to biosimilar adalimumab.

Design: Cross sectional survey

Setting: An anonymized, self-administered, web-based survey

Participants: The participants were drawn from members and non-members of either the National Rheumatoid Arthritis Society (NRAS), the National Axial Spondyloarthritis Society (NASS), Crohn's & Colitis UK (CCUK), or Psoriasis Association. Birdshot Uveitis Society and Olivia's Vision also signposted to the survey links.

Results: A total of 899 people living with various immune mediated inflammatory diseases participated in this survey. Thirty-four percent of respondents reported poor overall satisfaction with their biosimilar adalimumab after the switch, associated with complaints related to the switching process including lack of shared decision making, scarcity of information provided by or signposted to by the department instigating the switch as well as lack of training with the new injection device. Where training with the new device had been provided, there were significantly reduced reports of pain when

injecting the new biosimilar (odds ratio (*OR*) 0.20, 95% confidence interval (CI) 0.07 to 0.55), side effects (*OR* = 0.17, CI [0.06 to 0.47]) and difficulty in using the new injection device (*OR* = 0.25, CI [0.15 to 0.41]). Self-reported side effects were reduced by *OR* = 0.13, CI [0.05 to 0.38] when written information was provided by healthcare professionals and by *OR* = 0.15, CI [0.05 to 0.42] with provision of verbal information. Difficulty in using the new injection device was also reduced by provision of satisfactory information such as written documents (*OR* = 0.38, CI [0.23 to 0.63]) or by verbal communication with healthcare professionals (*OR* = 0.45, CI [0.27 to 0.73]). Finally, provision of satisfactory written or verbal information was associated with a reduction in any negative perception regarding symptom control with the new biosimilar by *OR* = 0.05, CI [0.004 to 0.57] and by *OR* = 0.15, [0.03 to 0.84] respectively.

Conclusions: Patient reported experiences of the process of switching from originator to biosimilar emphasise the importance of clear communication, training and information in order to optimise perception and maximize achievable outcomes with the new treatment.

Strengths and limitations of this study

- This patient survey of 899 subjects with an immune mediated inflammatory disease indicated that paucity of information provided during the switching process from anti-TNF originator to biosimilar was associated with reduced overall satisfaction with the biosimilar.
- Provision of training with the new biosimilar device significantly reduced reports of injection pain and difficulty in device use.
- Provision of written material and verbal instruction regarding the new biosimilar device significantly reduced reports of difficulty in device use.
- The study design included an open invitation to participate in the survey which may have had the limitation of introducing selection bias among respondents.
- Another limitation of the survey is that it was not designed or powered to assess any influence of the biologic formulation on the switching experience.

Introduction

Over the last two decades, biologic tumor necrosis factor (TNF) inhibitors such as adalimumab (ADA) have transformed achievable outcomes for patients with a wide variety of immune mediated inflammatory diseases including rheumatoid arthritis (RA), axial spondyloarthropathies (AS), skin psoriasis and psoriatic arthritis (PsA), Crohn's disease (CD) and other inflammatory bowel diseases such as ulcerative colitis (UC). However, the very high acquisition costs have resulted in varying degrees of restricted access across global healthcare economies. In 2017/2018, adalimumab cost the NHS in England £462m, of which £436m was spent on the drug's use in hospitals. In Scotland, the spend was in excess of £40m per annum, and in Wales, adalimumab cost secondary care £15m in 2016/2017[1]. When originator drugs approached patent expiry, biosimilar drugs emerged, and several have been approved for use in Europe. The first to be approved were infliximab and etanercept biosimilars, and more recently adalimumab biosimilars. A commissioning framework for use of best value biological medicines (including biosimilar medicines) was published by NHS England in September 2017, setting out NHS England's position and providing a framework to help commissioners develop plans for rapid and effective uptake of the best value biological medicines[2]. In September 2018, NHS England published their commissioning intentions for

adalimumab following the loss of patent exclusivity for Humira[3]. Guidance was issued to NHS Trusts and clinical commissioning groups (CCGs) with instructions that nine out of 10 new patients should be started on the best value biologic medicine within three months of a biosimilar launch and that at least 80% of existing patients should be switched or remain on the best value biologic (which could be the originator or a biosimilar) within 12 months. These directives came with the expectation of at least £150 million savings per year by 2021. The National Rheumatoid Arthritis Society (NRAS), National Axial Spondyloarthritis Society (NASS), Crohn's & Colitis UK (CCUK), and the Psoriasis Association together welcomed the news. In a joint statement, they said: "We welcome increased availability of effective treatment options for patients and understand the importance of the wise and careful use of NHS resources. The introduction of biosimilars for adalimumab brings opportunities for both patients and the NHS. However, it is vital that patients are fully informed about all the treatment options available to them and commissioners and health professionals adopt the principles of shared decision-making."

Although some previous studies have investigated the knowledge and perception of biosimilars among patients who had not yet switched to biosimilars from originators[4 5], the satisfaction and perception of the switching process among patients who have

already experienced it remains unclear. For people living with an immune mediated inflammatory disease whose disease has been well-controlled on a biologic anti-TNF originator, having to switch to an alternative agent may cause anxiety and even suspicion, especially if it is known that the reason for switching is to save money[6]. Therefore, it might be anticipated that provision of appropriate reassurance and relevant information during the switching process will have a substantial influence on achieving optimum outcomes and benefits.

In the present manuscript, we report the findings of a web-based survey designed by four UK patient organisations for people living with immune mediated inflammatory diseases for which biologic TNF inhibitors may be indicated, NRAS, NASS, Crohn's & Colitis UK and the Psoriasis Association UK. The survey was conducted in the UK to investigate the perceptions and experiences of patients about the process of switching from Humira to biosimilar adalimumab after the switch had been made.

Methods

Study design, setting and population

This was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations; NRAS, NASS, Crohn's & Colitis UK or Psoriasis Association UK. In addition, the Birdshot Uveitis Society and Olivia's Vision

also signposted to the survey links. The survey was undertaken for the purposes of service evaluation, prompted by the statement in NHS England's biosimilar commissioning framework that "shared decision making between clinical prescribers and patients will be vital if the best value, clinically effective medicines are to be used"[2]. The data were collected and analysed anonymously in subjects following a switch from originator to biosimilar adalimumab. The survey questions were designed to investigate the patients' experience of the switching process. Survey questions were developed by members of the patient organisations based upon issues determined to be of importance to patients. Face validity of the questions formulated was established by asking members of the relevant patient organisations to read through the questions and check them for sense and relevance.

The online survey was promoted via social media platforms, online communities and through the organisations' membership communications platforms. The patients were asked to complete the survey once they had completed the switching processes. People who lived outside the UK or were aged under 18 were excluded. This survey was designed by the four patient organisations and then distributed between April 4th and November 30th, 2019. The survey front page included information describing the survey and asked participants for voluntary participation. An electronic consent of voluntary

participation was sought from the respondents by clicking an “agree” button. All the responders were able to review and change their responses by scrolling up and down the page before submission. Cookies were used by the survey tool to minimize the chance of more than one response per computer.

A questionnaire comprising 27 questions was hosted on an electronic survey platform (Survey Monkey) and divided into three parts in the following manner: (1) characteristics of participants (questions 1-9, 26, 27), (2) individual experience of the switching process and perception of the new biosimilar (questions 10-23) , (3) individual opinion related to the switching process (questions 24, 25), (see survey questions in Supplementary Material). Most questions were formulated as closed, multiple-choice questions (MCQ), combined with free comments, with the exception of questions 13, 24, 25 which were full open questions. Findings from the free comments and open questions were not formally analysed as a part of the present work. The questionnaire did not ask for any personal identifying information. All the survey questions were developed to explore individual participants’ perceptions and satisfaction with the switching process from adalimumab originator to a biosimilar product. To explore the factors identified by the survey respondents which contributed to their perceptions of the switching process, we grouped them based on the level of satisfaction with the services provided by their

healthcare providers before switching, such as written information, verbal information and training for the new devices. Participants answering “4 (somewhat satisfied)” or “5 (very satisfied)” in question 12 were assigned to a category designated as “satisfied” and those responding that they were “1 (not at all satisfied)” or “2 (somewhat dissatisfied)” were assigned to a category of “dissatisfied”. Participants responding as “3 (neither)” or “not applicable (N/A)” were excluded from these categories. With respect to the participants’ perceptions of efficacy of the biosimilar, patients who answered “slightly better” and “much better” in questions 15 to 18 were assigned to a category of “better perception” and those who answered “slightly worse” and “much worse” were assigned to a category of “worse perception”. Those participants responding that the efficacy of the biosimilar was “the same” as originator or “not applicable (N/A)” were excluded from these categories.

Patient and Public Involvement

The survey questions were designed by members of the four national patient organisations and the survey itself was hosted on the websites of each of the four patient organisations. Members of the organisations and non-members visiting the website were invited to participate in the survey. Members of the four organisations made data available to the corresponding author, who is chief medical advisor to NRAS, and his

colleagues for analysis. Members of the patient organisations have commented on the findings, contributed to writing and have approved the final version of this manuscript.

Statistical analyses

The survey responses to the closed questions formulated as MCQs were collected and presented as number and percentages of responding patients. Variables were based on the choices of MCQ options. Disease activity was self-reported by the participants in question 9. Comparison of frequency of responses which showed “better” or “worse perception” between “the satisfied group” and “the dissatisfied group” were expressed as Odds ratios (*OR*) and 95% confidential intervals (95%CI). *P* values were assigned based on the chi-square test for categorical values when their expected values were higher than 10 and Fisher’s exact test was conducted if expected values of categorical values were smaller than with 10. *P* values less than 0.05 was considered statistically significant. A multiple categorical logistic regression analysis was used to select factors significantly associated with a positive perception of the new biosimilars following the switching process, after adjusting for gender, self-reported disease activity and biosimilar brands. All analyses were performed in JMP version 14.0 for windows.

Results

Participants

A total of 899 patients with different immune mediated inflammatory diseases participated in this survey. The largest response came from patients with Crohn's Disease (42%) followed by RA/JIA (25%), AS (19%) and skin psoriasis and PsA (13%). Most of the participants (52%) had been taking Humira® for between one to five years; about one fifth were recent users (<1y) and almost one fifth were long-term users (>5y). By self-evaluation of disease activity prior to switch, the majority (62%) were very well controlled, and 26% well controlled. Ten percent of participants had undertaken the survey just after their first injection of the new biosimilar. (Table 1).

The patients' experience and satisfaction with experience of switching process

Concerns about switching had been shared with the healthcare team by 43% of respondents and about a third of these (16 % of all survey participants) did not have their concerns satisfactorily dealt with. Over half of respondents (53%) reported not being asked for consent before switching and the majority of respondents reported poor overall satisfaction with their biosimilar adalimumab after the switch with only 8% "very satisfied", while 34% were "not at all satisfied" (Table 2).

Sixteen percent of participants were not at all satisfied with the written information about the switch to a biosimilar and 23% were dissatisfied with the verbal information received from their healthcare professionals. The lack of training with the new injection device was

also highlighted by 21% of respondents. Furthermore, more than half reported that they were not given an option to decline the switch or to delay it but rather to remain on originator (56% and 52%, respectively) (Figure 1).

After switching from originator to biosimilar, the most commonly reported problem was that of “worse pain” on injection with the biosimilar compared to originator. The injection pain was said to be “much worse” by 51% and “slightly worse” by 23% (Figure 1.). Ease of using the injection device was reported to be much worse by 22% of respondents. With respect to symptom control after the switch, 47% reported it to be the same or better (2%) than with originator. However, 20% reported that their symptoms were “much worse” (Figure 1). Respondents rating themselves as having higher disease activity tended to report greater dissatisfaction with all aspects of the switching process including written information, verbal information and training on the new injection devices (Table S1).

Comparison of proportion of patients with worse perception or better perception of the new biosimilars between those expressing satisfaction and dissatisfaction in the switching process

The proportion of participants with worse perception of the new biosimilar in term of side effects, ease of using the injection device and managing their symptoms was lower in the patients satisfied with the written (30% vs 63%, *OR* = 0.15, 95%CI [0.06 to 0.40];

40% vs 62%, *OR* = 0.35, 95%CI [0.21 to 0.58]; 28% vs 69.1%, *OR* = 0.11, 95%CI [0.02 to 0.49] respectively, all *P* values are < than 0.05) (Table S2a) and verbal information (33% vs 59%, *OR* =0.15, 95%CI [0.06 to 0.40]; 42% vs 60%, *OR* =0.45, 95%CI [0.28 to 0.72]; 32% vs 63%, *OR* =0.20, 95%CI [0.05 to 0.74] respectively, all *P* values are < than 0.05) (Table S2b). Aside from that, respondents satisfied with the training for the new injection device reported fewer side effects (37% vs 60%, *OR* =0.15, 95%CI [0.06 to 0.41]), less pain when injecting (70% vs 83%, *OR* =0.19, 95%CI [0.07 to 0.49]) and reduced difficulty in use of the injection device after the switching process (37% vs 66%, *OR* =0.24, 95%CI [0.15 to 0.40]) (all *P* values are < than 0.05) (Table S2c).

The benefits of informative communication and training in use of a new injection device on patients' perception of a new biosimilar

Results of the final logistic regression model incorporating gender, self-reported disease activity and biosimilar brand are summarized in Figure 2. The training in use of the new injection device was associated with a significant reduction in reported pain on administering the new biosimilar (*OR* = 0.20, 95%CI [0.07 to 0.55]), reporting of side effects (*OR* = 0.17, CI [0.06 to 0.47]) and difficulty in using the device (*OR* = 0.25, 95%CI [0.15 to 0.41]). Both satisfaction with written and verbal information about the switch to biosimilar provided by healthcare professionals was associated with fewer reported side

effects (*OR* = 0.13, 95%CI [0.05 to 0.38] in respect of the written information and *OR* = 0.15, 95%CI [0.05 to 0.42] in respect of the verbal information). Furthermore, provision of information perceived as being satisfactory significantly reduced participants' complaints regarding use of the new biosimilar injection device (*OR* = 0.38, 95%CI [0.23 to 0.63] in respect of the written information and OR= 0.45, 95%CI [0.27 to 0.73] in respect of the verbal information) as well as in managing their self-reported disease activity as compared with originator adalimumab (*OR* = 0.05, 95%CI [0.004 to 0.57] and *OR* = 0.15, 95%CI [0.03 to 0.84] respectively).

Discussion

A recent systematic literature review of patient experience of switching biologic treatment in patients with inflammatory arthritis or ulcerative colitis concluded that there is a sparsity of information regarding patient-reported experience of switching biologic treatment[7]. The present survey, designed and initiated by the patient organisations, addresses this issue. Our findings unequivocally highlight the importance of provision of clear, co-produced information about the switch to biosimilar as well as appropriate training in the use of a new injection device. The clear consequence of this best practice is a reduction in patient reported side effects and injection related pain as well as improved ease of using the injection device and reduction in any negative perceptions

regarding symptom control with the new biosimilar. The survey findings also suggest that switching from adalimumab originator to biosimilar was often done with suboptimal communication. It is thought likely that learnings regarding the importance of good communication and training will be generalizable to switching between other biologic originators and their biosimilars.

In order to be designated a biosimilar, a biologic has to demonstrate very vigorous similarities to the originator in terms of a wide range of parameters including antigen binding and antibody function as well as providing clinical trial data that demonstrates equivalent efficacy in an indication for which the originator has been approved[8-13]. From the perspective of healthcare economies, the potential savings generated by switching from originator to biosimilar products become considerable. For some healthcare systems for which biologics are purchased on the basis of a national or regional tender, such as Norway[14 15] or UK, for example, the originator drug price can also be lowered and compete in the tender process. While a more cost-effective biosimilar is very attractive for payers, it may appear much less so for patients who have responded well to an originator. They may initially be suspicious that they are being provided with a cheaper, and possibly less effective biologic alternative, purely to save money. While the complexity of clinical and biochemical evidence to support therapeutic equivalence

between biosimilar and originator has been established prior to approval of a biosimilar, this is unlikely to be known to the lay public and patients without a comprehensible explanation. And even then, there may be differences in biologic formulations, as there were in the case of this switch from Humira to adalimumab biosimilar, such as citrated versus non citrated, and the injection device itself, which might give rise to differences in individual experiences of the tolerability and ease of use between an originator or biosimilar. Of note, 22% of respondents reported the ease of using the injection device to be much worse following the switch to biosimilar. Such practical difficulties may have deleterious consequences for medication adherence, either intentionally or non-intentionally. Ideally, it is important for a patient to be able to familiarize themselves with the new biosimilar delivery device prior to any switch in biologic medication and to have the option to switch to a different device[16].

A limitation in the survey design and invitation to participate is in the potential for selection bias among responders, therefore the high proportion of respondents (about two thirds) expressing dissatisfaction with the switching process, may be an over-estimate of the wider population switched. Another limitation of the survey is that it was not designed or powered to assess any influence of the biologic formulation, such as citrated or non-citrated, on the switching experience.

So-called “nocebo” responses have been previously documented [14 17-21], and may be augmented by poor communication around the switching process. It is likely that nocebo responses might account for some of the reported dissatisfaction with the biosimilar in this large sample of survey respondents given that over a quarter were dissatisfied with either the verbal or written information communicated at the time of switch to adalimumab biosimilar. Our findings highlight the importance of healthcare professionals listening to their patients’ experiences, taking them seriously and acting to investigate and resolve issues satisfactorily when they are reported. Even when taking into consideration that there may have been selection bias among respondents, this study illustrates that specialist physicians and health care providers still have much to do in order to communicate the likelihood of maintained benefits to the individual being switched, and also the potential for widening access to expensive drugs, as well as the economic benefits for the wider health care economy. In fact, many patients accept the switch to biosimilars on the false premise of altruistic thinking that more people with the same health condition will be prescribed an anti-TNF. Unfortunately, this was not possible while NICE guidance set the threshold of high disease activity for access to a biological anti-TNF for people with certain immune mediated inflammatory diseases, for example, RA[22], Crohn’s disease[23] and skin psoriasis[24]. A challenge for the future will be whether the

biosimilars might regarded as sufficiently cost-effective to allow access for patients with moderately active disease, as is the case in many other European health economies.

As more biosimilar drugs are anticipated in the future, the learnings from this study should help inform best practice with respect to the switching process, involving good communication with the patient and meaningful shared decision making, thereby facilitating best achievable outcomes. Means to facilitate this include preparation of clearly presented written material, produced with patient involvement, explaining the therapeutic and safety equivalence of biosimilars to their originators as well as the reasons that there are associated cost savings, and the benefits these might provide for the individual, the clinical service and to broader society. Furthermore, healthcare professionals involved in the switch process, including physicians, nurses, pharmacists, and others, would benefit from training in use of different injection devices, provision of key verbal information and reassurance, and how to respond to frequently asked questions.

Table 1. Participant baseline characteristics

Characteristics	Participants (n= 899)	
Gender, n(%)		
Female	609	(68)
Male	277	(31)
Prefer not to say	6	(0.7)
Missing	7	(0.8)
Age, n (%)		
18-24	76	(8)
25-44	323	(36)
45-64	375	(42)
65+	118	(13)
Prefer not to say	7	(0.8)
Medical conditions, n (%)		
Crohn's Disease and Ulcerative colitis	376	(42)
Rheumatoid arthritis and Juvenile Idiopathic Arthritis	227	(25)
Axial spondyloarthritis including ankylosing spondylitis	170	(19)
Skin psoriasis and Psoriatic arthritis	112	(13)
Others	11	(1)
Missing	3	(0.3)
Period of Humira use before switching, n (%)		
Less than 1 year	204	(23)
More than 1 year to 5 years	468	(52)
More than 5 years	227	(25)
Patient-assessed disease activity prior to switch, n (%)		
Very well controlled	564	(63)
controlled well	225	(25)
Neither	85	(9)
Not controlled	12	(1)
Not controlled well at all	10	(1)
Not applicable	3	(0.3)
Number of the new biosimilar injections before survey, n (%)		
1	92	(10)
2 to 4	318	(35)
5 to 10	372	(41)
More than 10	110	(12)
Missing	7	(0.8)

Biosimilar, n (%)		
Imraldi®	561	(62)
Amgevita®	237	(26)
Hyrimoz®	56	(6)
Don't know/not sure	45	(5)

Values presented as n (%)

Table 2. Patient's experience in the process of switching

Questions	Answers	Participants (n=899)	
		n	(%)
1. Have you shared any concerns you may have with your consultant, specialist nurse, pharmacist, or GP?	Yes	388	(43)
	No	423	(47)
	I didn't know I could	87	(10)
2. Do you feel they have they offered you a satisfactory solution? ‡*	Yes, I was offered a switch back to my original treatment	65	(7)
	Yes, I was offered a switch to another treatment	41	(5)
	No	139	(15)
	Other free comment answers	139	(15)
3. Did your consultant, specialist nurse or pharmacist seek your consent to switch from Humira to a biosimilar?	Yes	359	(40)
	No	477	(53)
	Not sure / can't remember	63	(7)
4. Overall, how satisfied are you with your new biosimilar? †	Very satisfied	74	(8)
	Satisfied	177	(20)
	Neither	132	(15)
	Somewhat satisfied	202	(23)
	Not at all satisfied	307	(34)

‡The patients who answered "yes" in Question 1(n=388) then proceeded to Question 2. Four answers were missing in Question2. †Seven answers were missing in Question 4. *Patients responding to Q2 had the opportunity to do so in the form of free comment. Findings from the free comments and open questions were not formally analysed as a part of the present work.

Summary box

Section 1: What is already known on this topic

The very high acquisition costs of biologic TNF inhibitors such as Humira have resulted in restricted access across global healthcare economies.

In 2018, NHS England published their intentions with instructions that at least 80% of patients who use Humira should be switched to the best value biosimilar within 12 months.

The patient organisations welcomed NHS's policy, but they required that patients should be fully informed about the treatment options and health professionals adopt the principles of shared decision-making.

Section 2: What this study adds

Participants who responded to the survey request by the patient organisations reported poor satisfaction with the switching process to biosimilar due to paucity of information and training.

Where good information and training were provided, it was associated with reduction in self-reported side effects and injection related pain as well as greater ease of use of the injection device and management and control of symptoms.

Authors Contributions: PCT assumes overall responsibility for the work and all the reported data. CJ, AB, SD, SB, HA designed the patient survey and were involved in data collection. PCT and KK wrote the first draft of the manuscript. KK, DP-A and PCT analysed the data. All authors contributed to discussion and interpretation of the results, critically reviewed the manuscript and approved the final version to be submitted.

Transparency: PCT affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; there have been no discrepancies from the study as planned

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department and open for external participants; CJ reports grants from Abbvie, grants from Amgen, grants from Biogen, grants from Eli Lilly, grants and other from Frensius Kabi, grants from Gilead, grants from Janssen, grants from Medac, grants from Pfizer, grants from Roche, grants from UCB, grants from BMS, grants from Sanofi, outside the submitted work; AB reports grants from the following companies that are outside of and not related to the submitted paper: Abbvie, Amgen, Biogen, Eli Lilly, Fresenius Kabi, Gilead, Janssen, Medac, Pfizer, Roche, Sanofi, UCB, BMS; SD reports grants from AbbVie, grants from Biogen, grants from Eli Lilly, grants from Janssen-Cilag, grants from Novartis, grants from UCB, outside the submitted work; SB reports grants from Abbvie, grants from Amgen, grants from Celgene, grants from Janssen, grants from Gilead, grants from MSD, grants from Roche, grants from Sandoz, grants from Takeda, during the conduct of the study; HMc reports grants from Abbvie, grants from Almirall, grants from Amgen, grants from Celgene, grants from Eli Lilly, grants from Janssen, grants from LEO Pharma, grants from UCB, outside the submitted work; PCT reports personal fees from AbbVie, personal fees from Biogen, personal fees from Celltrion, personal fees from Fresenius Kabi, outside the submitted work

Ethical approval: Not required.

Data sharing: Raw anonymous data is available to researchers on application to the

patient organisations involved who will jointly assess any applications.

Dissemination Statement: The results will be shared with the study participants and the contributing patient organisations.

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third party to do any or all of the above.

Figure legends.

Figure 1.

Donut charts illustrating the percentage of patients expressing different levels of satisfaction with various experiences associated with the switching process.

Figure 2.

Adjusted odds rations illustrating the influence of training and information from healthcare professionals in improving perception of the new biosimilar. Adjusted odds ratio and 95% confidential intervals were calculated by a multiple categorical logistic regression analysis using gender, self-reported disease activity and biosimilar brands as adjusted variables. Data to the left of the adjusted odds ratio of 1 indicates a more favourable perception.

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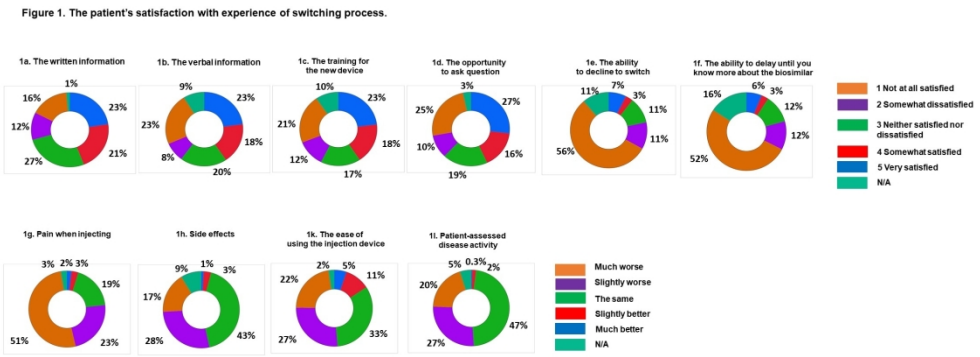

Figure 1. Donut charts illustrating the percentage of patients expressing different levels of satisfaction with various experiences associated with the switching process.

602x338mm (96 x 96 DPI)

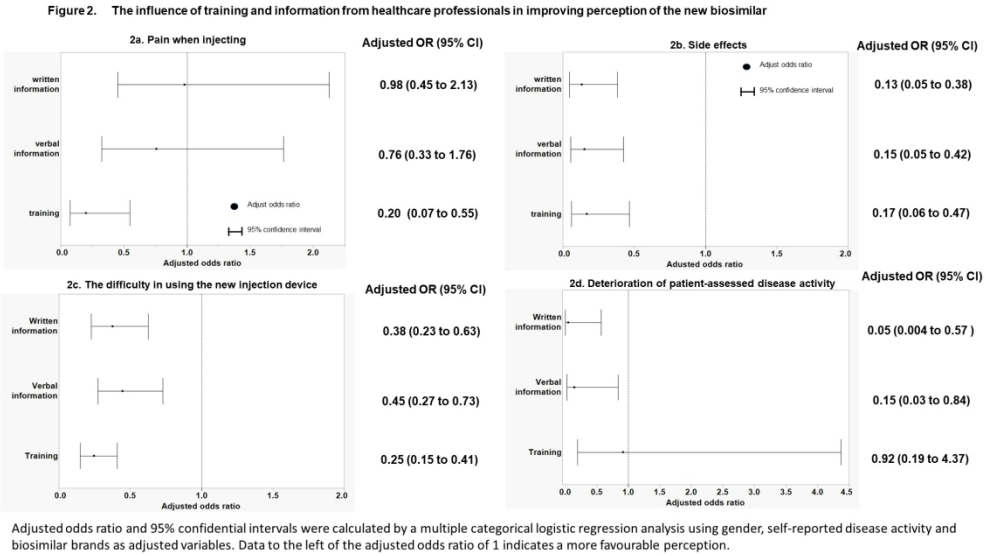

Figure 2. Adjusted odds rations illustrating the influence of training and information from healthcare professionals in improving perception of the new biosimilar. Adjusted odds ratio and 95% confidential intervals were calculated by a multiple categorical logistic regression analysis using gender, self-reported disease activity and biosimilar brands as adjusted variables. Data to the left of the adjusted odds ratio of 1 indicates a more favourable perception.

602x338mm (96 x 96 DPI)

TableS1. Comparison of characteristics of the participants between satisfied group and dissatisfied group with each experience in switching process.

Characteristics	The written information					The verbal information					The training for the new device				
	Satisfied group (N=394)		Dissatisfied group (N=249)		*p value*	Satisfied group (N=362)		Dissatisfied group (N=277)		*p value*	Satisfied group (N=364)		Dissatisfied group (N=295)		*p value*
Gender, n (%)					0.5201					0.3189					**0.00458***
Female	258	(66)	170	(69)		235	(65)	192	(70)		235	(65)	214	(74)	
Male	130	(33)	75	(30)		121	(34)	82	(30)		125	(34)	74	(26)	
Prefer not to say	4	(1)	1	(0)		4	(1)	1	(0)		3	(1)	2	(1)	
Age, n (%)					0.0546					**0.0003***					0.1091
18-24	28	(7)	24	(10)		25	(7)	27	(10)		26	(7)	26	(9)	
25-34	56	(14)	52	(21)		51	(14)	61	(22)		57	(16)	65	(22)	
35-44	70	(18)	50	(20)		55	(15)	59	(21)		71	(20)	62	(21)	
45-54	94	(24)	58	(23)		85	(23)	66	(24)		74	(20)	61	(21)	
55-64	80	(20)	40	(16)		78	(22)	38	(14)		77	(21)	45	(15)	
65+	61	(15)	24	(10)		63	(17)	25	(9)		54	(15)	35	(12)	
Prefer not to say	5	(1)	1	(0)		5	(1)	1	(0)		5	(1)	1	(0)	
Living areas, n (%)					0.3173					**0.0267***					0.9099
South East	101	(26)	69	(28)		96	(27)	72	(26)		95	(26)	80	(27)	
South West	75	(19)	43	(17)		76	(21)	48	(17)		68	(19)	60	(20)	
North East and Yorkshire	52	(13)	27	(11)		53	(15)	28	(10)		49	(13)	34	(12)	
Midlands	42	(11)	41	(16)		31	(9)	51	(18)		46	(13)	33	(11)	
East of England	46	(12)	17	(7)		37	(10)	28	(10)		39	(11)	28	(9)	
North West	31	(8)	17	(7)		26	(7)	18	(7)		28	(8)	19	(6)	
London	22	(6)	20	(8)		19	(5)	22	(8)		21	(6)	24	(8)	
Scotland	16	(4)	6	(2)		14	(4)	4	(1)		8	(2)	11	(4)	
Wales	6	(2)	6	(2)		7	(2)	4	(1)		6	(2)	4	(1)	

Northern Ireland	1	(0)	1	(0)		1	(0)	1	(0)		2	(1)	1	(0)	
Channel Islands	1	(0)	1	(0)		1	(0)	0	(0)		1	(0)	0	(0)	
Isle of Wight	1	(0)	1	(0)		1	(0)	1	(0)		1	(0)	1	(0)	
Medical conditions, n (%)					0.2988					0.0587					0.1358
CD	144	(37)	74	(30)		122	(34)	93	(34)		125	(35)	104	(35)	
RA/JIA	104	(27)	64	(26)		106	(29)	54	(19)		94	(26)	69	(23)	
AS	79	(20)	53	(21)		70	(19)	60	(22)		82	(23)	49	(17)	
PsA	22	(6)	24	(10)		23	(6)	30	(11)		22	(6)	30	(10)	
UC	25	(6)	19	(8)		23	(6)	26	(9)		21	(6)	24	(8)	
Psoriasis	15	(4)	11	(4)		13	(4)	11	(4)		14	(4)	12	(4)	
Others	3	(1)	4	(2)		4	(1)	3	(1)		4	(1)	7	(2)	
Period of Humira use before switching, n (%)					0.1228					**0.0095***					0.3304
3 months or less	14	(4)	14	(6)		12	(3)	11	(4)		14	(4)	16	(5)	
More than 3 months to 1 year	66	(17)	51	(20)		60	(17)	53	(19)		61	(17)	58	(20)	
More than 1 year to 5 years	208	(53)	130	(52)		177	(49)	159	(57)		188	(52)	152	(52)	
More than 5 years to 10 years	68	(17)	42	(17)		72	(20)	41	(15)		68	(19)	53	(18)	
More than 10 years	38	(10)	12	(5)		41	(11)	13	(5)		33	(9)	16	(5)	
Self-reported disease activity, n (%)					**0.0282***					**0.041***					**0.0358***
Very well controlled	243	(62)	157	(63)		229	(63)	174	(63)		226	(62)	190	(65)	
controlled well	104	(26)	64	(26)		99	(27)	69	(25)		84	(23)	80	(27)	
Neither	40	(10)	21	(8)		26	(7)	25	(9)		42	(12)	18	(6)	
Not controlled	1	(0)	6	(2)		2	(1)	7	(3)		4	(1)	5	(2)	
Not controlled well at all	6	(2)	0	(0)		6	(2)	0	(0)		7	(2)	1	(0)	

No. of injections of the new biosimilar before survey, n (%)					0.3279					0.4633				0.1015
1	35	(9)	27	(11)		32	(9)	29	(11)		37	(10)	31	(11)	
2	54	(14)	26	(11)		43	(12)	31	(11)		51	(14)	25	(9)	
3	55	(14)	25	(10)		49	(14)	28	(10)		48	(13)	31	(11)	
4	37	(9)	31	(13)		40	(11)	29	(11)		40	(11)	35	(12)	
5	25	(6)	26	(11)		22	(6)	21	(8)		16	(4)	30	(10)	
6	60	(15)	30	(12)		52	(14)	46	(17)		50	(14)	46	(16)	
7	18	(5)	12	(5)		15	(4)	13	(5)		13	(4)	11	(4)	
8	33	(8)	22	(9)		22	(6)	27	(10)		26	(7)	27	(9)	
9	10	(3)	8	(3)		12	(3)	9	(3)		9	(2)	8	(3)	
10	13	(3)	12	(5)		18	(5)	12	(4)		19	(5)	11	(4)	
More than 10	52	(13)	27	(11)		55	(15)	27	(10)		53	(15)	36	(12)	

CD, Crohn's Disease, RA, Rheumatoid arthritis, JIA, Juvenile Idiopathic Arthritis, AS, Axial spondyloarthritis including ankylosing spondylitis, PsA, Psoriatic arthritis, UC, Ulcerative colitis, Valuables presented as n (%), P values were assigned based on the chi-square test for categorical value when it's expected value is higher than 10 and Fisher's exact test was conducted if the expected values of categorical values were smaller than 10. *P values less than 0.05 was considered statistically significant.

Table S2a

		Comparison of proportion of patients with "worse perception" or "better perception" on the new biosimilars between those expressing satisfaction and dissatisfaction in the switching process									
		The written information									
		satisfied group (N=394)		dissatisfied group (N=249)		Neither (N=238)		N/A (N=13)		*unadjusted OR (95%CI)	*p value
Side effects	worse perception, n (%)	118	(30)	158	(63)	117	(49)	7	(54)	**0.15 (0.06-0.40)**	**<.0001†**
	better perception, n (%)	25	(6)	5	(2)	6	(3)	1	(8)		
	the same, n (%)	218	(56)	58	(23)	101	(42)	1	(8)		
	N/A, n (%)	31	(8)	28	(11)	14	(6)	4	(31)		
Pain when injecting	worse perception, n (%)	275	(70)	194	(78)	183	(77)	9	(69)	0.90 (0.45-1.81)	0.861
	better perception, n (%)	22	(6)	14	(6)	6	(3)	0	(0)		
	the same, n (%)	87	(22)	31	(13)	46	(19)	1	(8)		
	N/A, n (%)	8	(2)	9	(4)	3	(1)	3	(23)		
The ease of using the injection device	worse perception, n (%)	159	(40)	153	(62)	118	(50)	5	(38)	**0.35 (0.21-0.58)**	**<.0001†**
	better perception, n (%)	77	(20)	26	(10)	35	(15)	2	(15)		
	the same, n (%)	146	(37)	64	(26)	81	(34)	3	(23)		
	N/A, n (%)	11	(3)	5	(2)	3	(1)	3	(23)		
Managing symptoms	worse perception, n (%)	112	(28)	172	(69.1)	123	(52)	5	(38)	**0.11 (0.02-0.49)**	**0.0011†**
	better perception, n (%)	12	(3)	2	(0.8)	4	(2)	0	(0)		
	the same, n (%)	254	(64)	57	(22.9)	103	(44)	5	(38)		
	N/A, n (%)	16	(4)	18	(7.23)	6	(3)	3	(23)		

Valuables presented as n (%). *Comparison of frequency of responses with "worse perception" and "better perception" of the new biosimilar compared to originator between "satisfied group" and "dissatisfied group" with the experiences in the switching process to biosimilar were expressed as unadjusted odds ratios (OR), 95% confidential intervals (95%CI) and *p* values. Responses expressing "3 (neither)" or "not applicable (N/A)" in terms of satisfaction with the services in switching process and "the same" or "N/A" in terms of

the perception of the new biosimilar were excluded from the analysis. P values were assigned based on the chi-square test for categorical value when it's expected value is higher than 10 and Fisher's exact test was conducted if the expected values of categorical values were smaller than 10. †P values less than 0.05 was considered statistically significant.

Table S2b **Comparison of proportion of patients with "worse perception" or "better perception" on the new biosimilars between those expressing satisfaction and dissatisfaction in the switching process**

		The verbal information									
		Satisfied group (N=362)		Dissatisfied group (N=277)		Neither (N=175)		N/A (N=79)		*unadjusted OR (95%CI)	*p value
Side effects	Worse perception, n (%)	117	(33)	164	(59)	83	(47)	34	(43)	**0.15 (0.06-0.40)**	**<.0001†**
	Better perception, n (%)	24	(7)	5	(2)	5	(3)	3	(4)		
	The same, n (%)	192	(53)	79	(29)	76	(43)	31	(39)		
	N/A, n (%)	27	(8)	29	(10)	11	(6)	11	(14)		
Pain when injecting	Worse perception, n (%)	258	(71)	225	(82)	125	(72)	52	(66)	0.67 (0.30-1.50)	0.428
	Better perception, n (%)	17	(5)	10	(4)	13	(7)	3	(4)		
	The same, n (%)	76	(21)	34	(12)	34	(20)	20	(25)		
	N/A, n (%)	10	(3)	7	(3)	2	(1)	4	(5)		
The ease of using the injection device	Worse perception, n (%)	153	(42)	166	(60)	84	(48)	32	(41)	**0.45 (0.28-0.72)**	**0.0008†**
	Better perception, n (%)	66	(18)	32	(12)	26	(15)	16	(20)		
	The same, n (%)	130	(36)	73	(27)	63	(36)	27	(34)		
	N/A, n (%)	12	(3)	4	(1)	2	(1)	4	(5)		
Managing symptoms	Worse perception, n (%)	117	(32)	175	(63)	89	(51)	32	(41)	**0.20 (0.05-0.74)**	**0.0177†**
	Better perception, n (%)	10	(3)	3	(1)	(3)	(2)	2	(3)		
	The same, n (%)	221	(61)	76	(27)	(75)	(43)	45	(57)		
	N/A, n (%)	13	(4)	23	(8)	(7)	(4)	0	(0)		

Valuables presented as n (%). *Comparison of frequency of responses with "worse perception" and "better perception" of the new biosimilar compared to originator between “satisfied group” and “dissatisfied group” with the experiences in the switching process to biosimilar were expressed as unadjusted odds ratios (OR), 95% confidential intervals (95%CI) and *p* values. Responses expressing “3 (neither)” or “not applicable (N/A)“ in terms of satisfaction with the services in switching process and “the same” or “N/A” in terms of the perception of the new biosimilar were excluded from the analysis. P values were assigned based on the chi-square test for categorical value when it’s expected value is higher than 10 and Fisher’s exact test was conducted if the expected values of categorical values were smaller than 10. †P values less than 0.05 was considered statistically significant.

Table S2c

Comparison of proportion of patients with "worse perception" or "better perception" on the new biosimilars between those expressing satisfaction and dissatisfaction in the switching process

		The training									
		satisfied group (N=364)		dissatisfied group (N=295)		Neither (N=149)		N/A (N=86)		*unadjusted OR (95%CI)	*p value
Side effects	worse perception, n (%)	133	(37)	176	(60)	65	(44)	25	(29)	**0.15 (0.06-0.41)**	**<.0001†**
	better perception, n (%)	25	(7)	5	(2)	4	(3)	3	(4)		
	the same, n (%)	176	(48)	90	(31)	65	(44)	47	(55)		
	N/A, n (%)	29	(8)	24	(8)	15	(10)	10	(12)		
The ease of Pain when injecting	worse perception, n (%)	254	(70)	242	(83)	113	(76)	52	(60)	**0.19 (0.07-0.49)**	**0.0001†**
	better perception, n (%)	28	(8)	5	(2)	8	(5)	2	(2)		
	the same, n (%)	75	(21)	38	(13)	27	(18)	24	(28)		
	N/A, n (%)	6	(2)	8	(3)	1	(1)	8	(9)		
The ease of using the injection device	worse perception, n (%)	134	(37)	194	(66)	76	(51)	32	(37)	**0.24 (0.15-0.40)**	**<.0001†**
	better perception, n (%)	79	(22)	28	(10)	20	(14)	13	(15)		
	the same, n (%)	144	(40)	66	(22)	51	(34)	32	(37)		
	N/A, n (%)	6	(2)	6	(2)	1	(1)	9	(10)		
The ease of Managing symptoms	worse perception, n (%)	136	(37)	178	(60)	67	(45)	33	(38)	0.38 (0.11-1.30)	0.1412
	better perception, n (%)	8	(2)	4	(1)	4	(3)	2	(2)		
	the same, n (%)	201	(55)	97	(33)	73	(49)	46	(53)		
	N/A, n (%)	18	(5)	16	(5)	4	(3)	5	(6)		

Valuables presented as n (%). *Comparison of frequency of responses with "worse perception" and "better perception" of the new biosimilar compared to originator between "satisfied group" and "dissatisfied group" with the experiences in the switching process to biosimilar were expressed as unadjusted odds ratios (OR), 95% confidential intervals (95%CI) and *p* values. Responses expressing "3 (neither)" or "not applicable (N/A)" in terms of satisfaction with the services in switching process and "the same" or "N/A" in terms of the perception of the new biosimilar were excluded from the analysis. P values were assigned based on the chi-square test for categorical value when it's expected value is higher than 10 and Fisher's exact test was conducted if the expected values of categorical values were smaller than 10. †P values less than 0.05 was considered statistically significant.

We want to understand the recent experiences of people living in the UK who have switched from Humira to an adalimumab biosimilar medication.

If you haven't been asked to switch yet please note that we will keep this survey open for a few months so do feel that you can come back to it.

This survey is for only for people living in the UK aged 18+

1. Do you live in the UK?

- ○ Yes
- ○ No

2. What area of the UK do you live in?

- ○ Scotland
- ○ Wales
- ○ Northern Ireland
- ○ Isle of Man
- ○ Channel Islands
- ○ North East and Yorkshire
- ○ North West
- ○ Midlands
- ○ East of England
- ○ South West
- ○ South East
- ○ London

3. Were you being treated with Humira (adalimumab) during 2018?

- ○ Yes
- ○ No

4. What medical condition was your Humira primarily prescribed for?

- ○ Axial spondyloarthritis including ankylosing spondylitis (AS)
- ○ Crohn's Disease
- ○ Ulcerative colitis
- ○ Another form of IBD
- ○ Hidradenitis Suppurativa
- ○ Psoriasis
- ○ Psoriatic arthritis
- ○ Rheumatoid arthritis (RA)
- ○ Juvenile Idiopathic Arthritis (JIA)
- ○ Uveitis
- ○ Other (please specify)

5. Have you switched from Humira to an adalimumab biosimilar?

- ○ Yes
- ○ No

6. Did your consultant, specialist nurse or pharmacist seek your consent to switch from Humira to a biosimilar?

- ○ Yes
- ○ No
- ○ Not sure / can't remember

7. Which biosimilar medication have you switched to?

- ○ Amgevita
- ○ Hulio
- ○ Hyrimoz
- ○ Imraldi
- ○ Don't know/not sure

8. How long were you taking Humira prior to being switched?

- ○ 3 months or less
- ○ More than 3 months to 1 year
- ○ More than 1 year to 5 years
- ○ More than 5 years to 10 years
- ○ More than 10 years

9. Thinking about the time you were being treated with Humira (adalimumab) how well do you feel your disease was controlled? Please use the scale of 1 to 5 where 1 means your condition was not controlled well at all and 5 means very well controlled

Not at all satisfied	Somewhat dissatisfied	Neither satisfied nor dissatisfied	Somewhat satisfied	Very satisfied	N/A
○	○	○	○	○	○

Now, thinking about the process of switching

10. In which of the following ways did you first hear you may be asked to switch to a biosimilar?

- ○ I was told about the potential to switch face to face in clinic by my consultant
- ○ I was told about the potential to switch face to face in clinic by my specialist nurse
- ○ I was invited to a patient information meeting about biosimilars
- ○ I received a letter from the hospital
- ○ I received a letter from the homecare delivery company
- ○ I received a telephone call from the specialist nurse
- ○ I received a telephone call from the homecare delivery company
- ○ I received a telephone call from the hospital pharmacy
- ○ I received no prior notice of my treatment being switched
- ○ Other (please specify)

11. Thinking about what you heard about switching, which of the following information did you pick up from what you were told or given in writing?

- ○ Switching to biosimilars will save the NHS money
- ○ Biosimilars are almost identical and I should notice no difference in my symptoms or side effects
- ○ Switching to biosimilars will mean my hospital department would benefit and might be able to offer improved services to patients
- ○ Switching to biosimilars means more patients would be able to get prescribed these medications
- ○ I had a choice and could choose not to switch if I preferred
- ○ I would be switched to a biosimilar medication and there were no other options
- ○ I was given links to more information on biosimilars (e.g. on patient organisation websites)
- ○ Who to contact with any queries I may have about biosimilars
- ○ Other (please specify)

12. Thinking about your experience of the switching process, how would you rate your satisfaction with...

	Not at all satisfied	Somewhat dissatisfied	Neither satisfied nor dissatisfied	Somewhat satisfied	Very satisfied	N/A
The written information you received about the switch to a biosimilar	○	○	○	○	○	○
The verbal information you received about the switch from your healthcare professional	○	○	○	○	○	○
The opportunity to ask questions	○	○	○	○	○	○
The training for the new device	○	○	○	○	○	○
The ability to decline to switch	○	○	○	○	○	○
The ability to delay switching until you knew more about the biosimilar	○	○	○	○	○	○

13. What, if anything, do you think could have been done better to help the switching process run more smoothly?

Now, thinking about the biosimilar you were switched to

14. How many injections of the new biosimilar would you estimate you have taken so far?

- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 7
- ○ 8
- ○ 9
- ○ 10
- ○ More than 10

15. Thinking about how you feel the new biosimilar is working for you in terms of managing your symptoms compared with Humira would you say it is...

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

16. And what about in terms of side effects?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

17. And pain when injecting?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

18. And the ease of using the injection device?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

19. And the ease of accessing the injection device via the external packaging?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

20. And the Homecare company arrangements?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

21. And overall, how satisfied are you with your new biosimilar? Scale of 1 to 5 where 5 is very satisfied and 1 is not at all satisfied

Not at all satisfied	Somewhat satisfied	Neither	Satisfied	Very satisfied
○	○	○	○	○

And why do you say that?

22. And have you shared any concerns you may have with your consultant, specialist nurse, pharmacist, physiotherapist or GP?

○ Yes
○ No
○ I didn't know I could

23. And do you feel they have they offered you a satisfactory solution?

○ Yes, I was offered a switch back to my original treatment
○ Yes, I was offered a switch to another treatment
○ No
○ Other (please specify)

24. What do you think is most important for hospitals to be aware of as part of the switching process for new patients going forward?

25. Do you have any other comments about your experience of the biosimilar switching process?

Thank you for your time, can we just ask you for some information about yourself.

26. Gender

- ○ Female
- ○ Male
- ○ Other
- ○ Prefer not to say

27. Age

- ○ 18-24
- ○ 25-34
- ○ 35-44
- ○ 45-54
- ○ 55-64
- ○ 65+
- ○ Prefer not to say

If you are experiencing side effects with any medication please do remember anyone can report suspected side effects using the Yellow Card Scheme. Visit: mhra.gov.uk/yellowcard or call 0808 100 3352 for a paper form.

Do also speak to your rheumatologist or rheumatology nurse.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P.4 line5
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P.4 line12 to P.5 line11
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P.7 line2 to P.9 line7
Objectives	3	State specific objectives, including any prespecified hypotheses	P.9 line11 to 13
Methods			
Study design	4	Present key elements of study design early in the paper	P.9 line16 to 17
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P.10 line1 to 12, and P.10 line16 to P.11 line5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P.10 line 13 to 16, and P.12 line16 to P.13 line4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P.11 line18 to P.12 line17
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P.11 line 6 to 17
Bias	9	Describe any efforts to address potential sources of bias	Not applicable because this was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations.
Study size	10	Explain how the study size was arrived at	Not applicable because this was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Not applicable because we did not handle with quantitative variables.

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P. 13 line6 to 18
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable because we did not examine subgroups and interactions
		(*c*) Explain how missing data were addressed	Not described.
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	Not applicable because this was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations.
		(*e*) Describe any sensitivity analyses	Not applicable because we did not conduct any sensitivity analyses
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P.14 line3 to 4
		(b) Give reasons for non-participation at each stage	Not applicable because this was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations.
		(c) Consider use of a flow diagram	Not applicable because this was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P.14 line 4 to 10
		(b) Indicate number of participants with missing data for each variable of interest	Described in Table 1 and 2.
Outcome data	15*	Report numbers of outcome events or summary measures	Not applicable because all participants experienced the switching process.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	P.15 line18 to P.17 line10
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable because continuous variables were not analysed

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable because we did not evaluate the relative risk
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable because we did not conduct analysis of subgroup and interactions, and sensitivity analyses
Discussion			
Key results	18	Summarise key results with reference to study objectives	P.17 line16 to p.18 line5
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P.19 line16 to P.20 line3
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P.20 line4 to P.21 line5
Generalisability	21	Discuss the generalisability (external validity) of the study results	p.21 line6 to 16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p.25 line 10 to 11

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

The influence of information provided prior to switching from Humira to biosimilar adalimumab on UK patients' satisfaction: a cross sectional survey by patient organisations.

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Research Article

The influence of information provided prior to switching from Humira to biosimilar adalimumab on UK patients' satisfaction: a cross sectional survey by patient organisations.

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The number of figures: 2

The number of supplemental tables: 2

Other supplementary material: patient survey questionnaire: 1

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Abstract

Objectives: To investigate the perceptions and experiences of people with specific immune mediated inflammatory diseases during the process of switching from Humira to biosimilar adalimumab.

Design: Cross sectional survey

Setting: An anonymized, self-administered, web-based survey

Participants: The participants were drawn from members and non-members of either the National Rheumatoid Arthritis Society (NRAS), the National Axial Spondyloarthritis Society (NASS), Crohn's & Colitis UK (CCUK), or Psoriasis Association. Birdshot Uveitis Society and Olivia's Vision also signposted to the survey links.

Results: A total of 899 people living with various immune mediated inflammatory diseases participated in this survey. Thirty-four percent of respondents reported poor overall satisfaction with their biosimilar adalimumab after the switch, associated with complaints related to the switching process including lack of shared decision making, scarcity of information provided by or signposted to by the department instigating the switch as well as lack of training with the new injection device. Where training with the new device had been provided, there were significantly reduced reports of pain when

injecting the new biosimilar (odds ratio (*OR*) 0.20, 95% confidence interval (CI) 0.07 to 0.55), side effects (*OR* = 0.17, CI [0.06 to 0.47]) and difficulty in using the new injection device (*OR* = 0.25, CI [0.15 to 0.41]). Self-reported side effects were reduced by *OR* = 0.13, CI [0.05 to 0.38] when written information was provided by healthcare professionals and by *OR* = 0.15, CI [0.05 to 0.42] with provision of verbal information. Difficulty in using the new injection device was also reduced by provision of satisfactory information such as written documents (*OR* = 0.38, CI [0.23 to 0.63]) or by verbal communication with healthcare professionals (*OR* = 0.45, CI [0.27 to 0.73]). Finally, provision of satisfactory written or verbal information was associated with a reduction in any negative perception regarding symptom control with the new biosimilar by *OR* = 0.05, CI [0.004 to 0.57] and by *OR* = 0.15, [0.03 to 0.84] respectively.

Conclusions: Patient reported experiences of the process of switching from originator to biosimilar emphasise the importance of clear communication, training and information in order to optimise perception and maximize achievable outcomes with the new treatment.

Strengths and limitations of this study

- This was an anonymized, self-administered, web-based survey designed by members of patient organisations for the purposes of service evaluation following a switch from originator to biosimilar adalimumab.
- Survey questions were designed to investigate the patients' experience of the switching process.
- Face validity of the survey questions was established by asking members of the relevant patient organisations to read through the questions and check them for sense and relevance.
- The study design included an open invitation to participate in the survey which may have had the limitation of introducing selection bias among respondents.
- Another limitation of the survey is that it was not designed or powered to assess any influence of the biologic formulation on the switching experience.

Introduction

Over the last two decades, biologic tumor necrosis factor (TNF) inhibitors such as adalimumab (ADA) have transformed achievable outcomes for patients with a wide variety of immune mediated inflammatory diseases including rheumatoid arthritis (RA), axial spondyloarthropathies (AS), skin psoriasis and psoriatic arthritis (PsA), Crohn's disease (CD) and other inflammatory bowel diseases such as ulcerative colitis (UC). However, the very high acquisition costs have resulted in varying degrees of restricted access across global healthcare economies. In 2017/2018, adalimumab cost the NHS in England £462m, of which £436m was spent on the drug's use in hospitals. In Scotland, the spend was in excess of £40m per annum, and in Wales, adalimumab cost secondary care £15m in 2016/2017[1]. When originator drugs approached patent expiry, biosimilar drugs emerged, and several have been approved for use in Europe. The first to be approved were infliximab and etanercept biosimilars, and more recently adalimumab biosimilars. A commissioning framework for use of best value biological medicines (including biosimilar medicines) was published by NHS England in September 2017, setting out NHS England's position and providing a framework to help commissioners develop plans for rapid and effective uptake of the best value biological medicines[2]. In September 2018, NHS England published their commissioning intentions for

adalimumab following the loss of patent exclusivity for Humira[3]. Guidance was issued to NHS Trusts and clinical commissioning groups (CCGs) with instructions that nine out of 10 new patients should be started on the best value biologic medicine within three months of a biosimilar launch and that at least 80% of existing patients should be switched or remain on the best value biologic (which could be the originator or a biosimilar) within 12 months. These directives came with the expectation of at least £150 million savings per year by 2021. The National Rheumatoid Arthritis Society (NRAS), National Axial Spondyloarthritis Society (NASS), Crohn's & Colitis UK (CCUK), and the Psoriasis Association together welcomed the news. In a joint statement, they said: "We welcome increased availability of effective treatment options for patients and understand the importance of the wise and careful use of NHS resources. The introduction of biosimilars for adalimumab brings opportunities for both patients and the NHS. However, it is vital that patients are fully informed about all the treatment options available to them and commissioners and health professionals adopt the principles of shared decision-making."

Although some previous studies have investigated the knowledge and perception of biosimilars among patients who had not yet switched to biosimilars from originators[4 5], the satisfaction and perception of the switching process among patients who have

already experienced it remains unclear. For people living with an immune mediated inflammatory disease whose disease has been well-controlled on a biologic anti-TNF originator, having to switch to an alternative agent may cause anxiety and even suspicion, especially if it is known that the reason for switching is to save money[6]. Therefore, it might be anticipated that provision of appropriate reassurance and relevant information during the switching process will have a substantial influence on achieving optimum outcomes and benefits.

In the present manuscript, we report the findings of a web-based survey designed by four UK patient organisations for people living with immune mediated inflammatory diseases for which biologic TNF inhibitors may be indicated, NRAS, NASS, Crohn's & Colitis UK and the Psoriasis Association UK. The survey was conducted in the UK to investigate the perceptions and experiences of patients about the process of switching from Humira to biosimilar adalimumab after the switch had been made.

Methods

Study design, setting and population

This was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations; NRAS, NASS, Crohn's & Colitis UK or Psoriasis Association UK. In addition, the Birdshot Uveitis Society and Olivia's Vision

also signposted to the survey links. The survey was undertaken for the purposes of service evaluation, prompted by the statement in NHS England's biosimilar commissioning framework that "shared decision making between clinical prescribers and patients will be vital if the best value, clinically effective medicines are to be used"[2]. The data were collected and analysed anonymously in subjects following a switch from originator to biosimilar adalimumab. The survey questions were designed to investigate the patients' experience of the switching process. Survey questions were developed by members of the patient organisations based upon issues determined to be of importance to patients. Face validity of the questions formulated was established by asking members of the relevant patient organisations to read through the questions and check them for sense and relevance.

The online survey was promoted via social media platforms, online communities and through the organisations' membership communications platforms. The patients were asked to complete the survey once they had completed the switching processes. People who lived outside the UK or were aged under 18 were excluded. This survey was designed by the four patient organisations and then distributed between April 4th and November 30th, 2019. The survey front page included information describing the survey and asked participants for voluntary participation. An electronic consent of voluntary

participation was sought from the respondents by clicking an “agree” button. All the responders were able to review and change their responses by scrolling up and down the page before submission. Cookies were used by the survey tool to minimize the chance of more than one response per computer.

A questionnaire comprising 27 questions was hosted on an electronic survey platform (Survey Monkey) and divided into three parts in the following manner: (1) characteristics of participants (questions 1-9, 26, 27), (2) individual experience of the switching process and perception of the new biosimilar (questions 10-23) , (3) individual opinion related to the switching process (questions 24, 25), (see survey questions in Supplementary Material). Most questions were formulated as closed, multiple-choice questions (MCQ), combined with free comments, with the exception of questions 13, 24, 25 which were full open questions. Findings from the free comments and open questions were not formally analysed as a part of the present work. The questionnaire did not ask for any personal identifying information. All the survey questions were developed to explore individual participants’ perceptions and satisfaction with the switching process from adalimumab originator to a biosimilar product. To explore the factors identified by the survey respondents which contributed to their perceptions of the switching process, we grouped them based on the level of satisfaction with the services provided by their

healthcare providers before switching, such as written information, verbal information and training for the new devices. Participants answering “4 (somewhat satisfied)” or “5 (very satisfied)” in question 12 were assigned to a category designated as “satisfied” and those responding that they were “1 (not at all satisfied)” or “2 (somewhat dissatisfied)” were assigned to a category of “dissatisfied”. Participants responding as “3 (neither)” or “not applicable (N/A)” were excluded from these categories. With respect to the participants’ perceptions of efficacy of the biosimilar, patients who answered “slightly better” and “much better” in questions 15 to 18 were assigned to a category of “better perception” and those who answered “slightly worse” and “much worse” were assigned to a category of “worse perception”. Those participants responding that the efficacy of the biosimilar was “the same” as originator or “not applicable (N/A)” were excluded from these categories.

Patient and Public Involvement

The survey questions were designed by members of the four national patient organisations and the survey itself was hosted on the websites of each of the four patient organisations. Members of the organisations and non-members visiting the website were invited to participate in the survey. Members of the four organisations made data available to the corresponding author, who is chief medical advisor to NRAS, and his

colleagues for analysis. Members of the patient organisations have commented on the findings, contributed to writing and have approved the final version of this manuscript.

Statistical analyses

The survey responses to the closed questions formulated as MCQs were collected and presented as number and percentages of responding patients. Variables were based on the choices of MCQ options. Disease activity was self-reported by the participants in question 9. Comparison of frequency of responses which showed “better” or “worse perception” between “the satisfied group” and “the dissatisfied group” were expressed as Odds ratios (*OR*) and 95% confidential intervals (95%CI). *P* values were assigned based on the chi-square test for categorical values when their expected values were higher than 10 and Fisher’s exact test was conducted if expected values of categorical values were smaller than with 10. *P* values less than 0.05 was considered statistically significant. A multiple categorical logistic regression analysis was used to select factors significantly associated with a positive perception of the new biosimilars following the switching process, after adjusting for gender, self-reported disease activity and biosimilar brands. All analyses were performed in JMP version 14.0 for windows.

Results

Participants

A total of 899 patients with different immune mediated inflammatory diseases participated in this survey. The largest response came from patients with Crohn's Disease (42%) followed by RA/JIA (25%), AS (19%) and skin psoriasis and PsA (13%). Most of the participants (52%) had been taking Humira® for between one to five years; about one fifth were recent users (<1y) and almost one fifth were long-term users (>5y). By self-evaluation of disease activity prior to switch, the majority (62%) were very well controlled, and 26% well controlled. Ten percent of participants had undertaken the survey just after their first injection of the new biosimilar. (Table 1).

The patients' experience and satisfaction with experience of switching process

Concerns about switching had been shared with the healthcare team by 43% of respondents and about a third of these (16 % of all survey participants) did not have their concerns satisfactorily dealt with. Over half of respondents (53%) reported not being asked for consent before switching and the majority of respondents reported poor overall satisfaction with their biosimilar adalimumab after the switch with only 8% "very satisfied", while 34% were "not at all satisfied" (Table 2).

Sixteen percent of participants were not at all satisfied with the written information about the switch to a biosimilar and 23% were dissatisfied with the verbal information received from their healthcare professionals. The lack of training with the new injection device was

also highlighted by 21% of respondents. Furthermore, more than half reported that they were not given an option to decline the switch or to delay it but rather to remain on originator (56% and 52%, respectively) (Figure 1).

After switching from originator to biosimilar, the most commonly reported problem was that of “worse pain” on injection with the biosimilar compared to originator. The injection pain was said to be “much worse” by 51% and “slightly worse” by 23% (Figure 1.). Ease of using the injection device was reported to be much worse by 22% of respondents. With respect to symptom control after the switch, 47% reported it to be the same or better (2%) than with originator. However, 20% reported that their symptoms were “much worse” (Figure 1). Respondents rating themselves as having higher disease activity tended to report greater dissatisfaction with all aspects of the switching process including written information, verbal information and training on the new injection devices (Table S1).

Comparison of proportion of patients with worse perception or better perception of the new biosimilars between those expressing satisfaction and dissatisfaction in the switching process

The proportion of participants with worse perception of the new biosimilar in term of side effects, ease of using the injection device and managing their symptoms was lower in the patients satisfied with the written (30% vs 63%, *OR* = 0.15, 95%CI [0.06 to 0.40];

40% vs 62%, *OR* = 0.35, 95%CI [0.21 to 0.58]; 28% vs 69.1%, *OR* = 0.11, 95%CI [0.02 to 0.49] respectively, all *P* values are < than 0.05) (Table S2a) and verbal information (33% vs 59%, *OR* =0.15, 95%CI [0.06 to 0.40]; 42% vs 60%, *OR* =0.45, 95%CI [0.28 to 0.72]; 32% vs 63%, *OR* =0.20, 95%CI [0.05 to 0.74] respectively, all *P* values are < than 0.05) (Table S2b). Aside from that, respondents satisfied with the training for the new injection device reported fewer side effects (37% vs 60%, *OR* =0.15, 95%CI [0.06 to 0.41]), less pain when injecting (70% vs 83%, *OR* =0.19, 95%CI [0.07 to 0.49]) and reduced difficulty in use of the injection device after the switching process (37% vs 66%, *OR* =0.24, 95%CI [0.15 to 0.40]) (all *P* values are < than 0.05) (Table S2c).

The benefits of informative communication and training in use of a new injection device on patients' perception of a new biosimilar

Results of the final logistic regression model incorporating gender, self-reported disease activity and biosimilar brand are summarized in Figure 2. The training in use of the new injection device was associated with a significant reduction in reported pain on administering the new biosimilar (*OR* = 0.20, 95%CI [0.07 to 0.55]), reporting of side effects (*OR* = 0.17, CI [0.06 to 0.47]) and difficulty in using the device (*OR* = 0.25, 95%CI [0.15 to 0.41]). Both satisfaction with written and verbal information about the switch to biosimilar provided by healthcare professionals was associated with fewer reported side

effects (*OR* = 0.13, 95%CI [0.05 to 0.38] in respect of the written information and *OR* = 0.15, 95%CI [0.05 to 0.42] in respect of the verbal information). Furthermore, provision of information perceived as being satisfactory significantly reduced participants' complaints regarding use of the new biosimilar injection device (*OR* = 0.38, 95%CI [0.23 to 0.63] in respect of the written information and OR= 0.45, 95%CI [0.27 to 0.73] in respect of the verbal information) as well as in managing their self-reported disease activity as compared with originator adalimumab (*OR* = 0.05, 95%CI [0.004 to 0.57] and *OR* = 0.15, 95%CI [0.03 to 0.84] respectively).

Discussion

A recent systematic literature review of patient experience of switching biologic treatment in patients with inflammatory arthritis or ulcerative colitis concluded that there is a sparsity of information regarding patient-reported experience of switching biologic treatment[7]. The present survey, designed and initiated by the patient organisations, addresses this issue. Our findings unequivocally highlight the importance of provision of clear, co-produced information about the switch to biosimilar as well as appropriate training in the use of a new injection device. The clear consequence of this best practice is a reduction in patient reported side effects and injection related pain as well as improved ease of using the injection device and reduction in any negative perceptions

regarding symptom control with the new biosimilar. The survey findings also suggest that switching from adalimumab originator to biosimilar was often done with suboptimal communication. It is thought likely that learnings regarding the importance of good communication and training will be generalizable to switching between other biologic originators and their biosimilars.

In order to be designated a biosimilar, a biologic has to demonstrate very vigorous similarities to the originator in terms of a wide range of parameters including antigen binding and antibody function as well as providing clinical trial data that demonstrates equivalent efficacy in an indication for which the originator has been approved[8-13]. From the perspective of healthcare economies, the potential savings generated by switching from originator to biosimilar products become considerable. For some healthcare systems for which biologics are purchased on the basis of a national or regional tender, such as Norway[14 15] or UK, for example, the originator drug price can also be lowered and compete in the tender process. While a more cost-effective biosimilar is very attractive for payers, it may appear much less so for patients who have responded well to an originator. They may initially be suspicious that they are being provided with a cheaper, and possibly less effective biologic alternative, purely to save money. While the complexity of clinical and biochemical evidence to support therapeutic equivalence

between biosimilar and originator has been established prior to approval of a biosimilar, this is unlikely to be known to the lay public and patients without a comprehensible explanation. And even then, there may be differences in biologic formulations, as there were in the case of this switch from Humira to adalimumab biosimilar, such as citrated versus non citrated, and the injection device itself, which might give rise to differences in individual experiences of the tolerability and ease of use between an originator or biosimilar. Of note, 22% of respondents reported the ease of using the injection device to be much worse following the switch to biosimilar. Such practical difficulties may have deleterious consequences for medication adherence, either intentionally or non-intentionally. Ideally, it is important for a patient to be able to familiarize themselves with the new biosimilar delivery device prior to any switch in biologic medication and to have the option to switch to a different device[16].

A limitation in the survey design and invitation to participate is in the potential for selection bias among responders, therefore the high proportion of respondents (about two thirds) expressing dissatisfaction with the switching process, may be an over-estimate of the wider population switched. Another limitation of the survey is that it was not designed or powered to assess any influence of the biologic formulation, such as citrated or non-citrated, on the switching experience.

So-called “nocebo” responses have been previously documented [14 17-21], and may be augmented by poor communication around the switching process. It is likely that nocebo responses might account for some of the reported dissatisfaction with the biosimilar in this large sample of survey respondents given that over a quarter were dissatisfied with either the verbal or written information communicated at the time of switch to adalimumab biosimilar. Our findings highlight the importance of healthcare professionals listening to their patients’ experiences, taking them seriously and acting to investigate and resolve issues satisfactorily when they are reported. Even when taking into consideration that there may have been selection bias among respondents, this study illustrates that specialist physicians and health care providers still have much to do in order to communicate the likelihood of maintained benefits to the individual being switched, and also the potential for widening access to expensive drugs, as well as the economic benefits for the wider health care economy. In fact, many patients accept the switch to biosimilars on the false premise of altruistic thinking that more people with the same health condition will be prescribed an anti-TNF. Unfortunately, this was not possible while NICE guidance set the threshold of high disease activity for access to a biological anti-TNF for people with certain immune mediated inflammatory diseases, for example, RA[22], Crohn’s disease[23] and skin psoriasis[24]. A challenge for the future will be whether the

biosimilars might regarded as sufficiently cost-effective to allow access for patients with moderately active disease, as is the case in many other European health economies.

As more biosimilar drugs are anticipated in the future, the learnings from this study should help inform best practice with respect to the switching process, involving good communication with the patient and meaningful shared decision making, thereby facilitating best achievable outcomes. Means to facilitate this include preparation of clearly presented written material, produced with patient involvement, explaining the therapeutic and safety equivalence of biosimilars to their originators as well as the reasons that there are associated cost savings, and the benefits these might provide for the individual, the clinical service and to broader society. Furthermore, healthcare professionals involved in the switch process, including physicians, nurses, pharmacists, and others, would benefit from training in use of different injection devices, provision of key verbal information and reassurance, and how to respond to frequently asked questions.

Table 1. Participant baseline characteristics

Characteristics	Participants (n= 899)	
Gender, n(%)		
Female	609	(68)
Male	277	(31)
Prefer not to say	6	(0.7)
Missing	7	(0.8)
Age, n (%)		
18-24	76	(8)
25-44	323	(36)
45-64	375	(42)
65+	118	(13)
Prefer not to say	7	(0.8)
Medical conditions, n (%)		
Crohn's Disease and Ulcerative colitis	376	(42)
Rheumatoid arthritis and Juvenile Idiopathic Arthritis	227	(25)
Axial spondyloarthritis including ankylosing spondylitis	170	(19)
Skin psoriasis and Psoriatic arthritis	112	(13)
Others	11	(1)
Missing	3	(0.3)
Period of Humira use before switching, n (%)		
Less than 1 year	204	(23)
More than 1 year to 5 years	468	(52)
More than 5 years	227	(25)
Patient-assessed disease activity prior to switch, n (%)		
Very well controlled	564	(63)
controlled well	225	(25)
Neither	85	(9)
Not controlled	12	(1)
Not controlled well at all	10	(1)
Not applicable	3	(0.3)
Number of the new biosimilar injections before survey, n (%)		
1	92	(10)
2 to 4	318	(35)
5 to 10	372	(41)
More than 10	110	(12)
Missing	7	(0.8)

Biosimilar, n (%)		
Imraldi®	561	(62)
Amgevita®	237	(26)
Hyrimoz®	56	(6)
Don't know/not sure	45	(5)

Values presented as n (%)

Table 2. Patient's experience in the process of switching

Questions	Answers	Participants (n=899)	
		n	(%)
1. Have you shared any concerns you may have with your consultant, specialist nurse, pharmacist, or GP?	Yes	388	(43)
	No	423	(47)
	I didn't know I could	87	(10)
2. Do you feel they have they offered you a satisfactory solution? ‡*	Yes, I was offered a switch back to my original treatment	65	(7)
	Yes, I was offered a switch to another treatment	41	(5)
	No	139	(15)
	Other free comment answers	139	(15)
3. Did your consultant, specialist nurse or pharmacist seek your consent to switch from Humira to a biosimilar?	Yes	359	(40)
	No	477	(53)
	Not sure / can't remember	63	(7)
4. Overall, how satisfied are you with your new biosimilar? †	Very satisfied	74	(8)
	Satisfied	177	(20)
	Neither	132	(15)
	Somewhat satisfied	202	(23)
	Not at all satisfied	307	(34)

‡The patients who answered "yes" in Question 1(n=388) then proceeded to Question 2. Four answers were missing in Question2. †Seven answers were missing in Question 4. *Patients responding to Q2 had the opportunity to do so in the form of free comment. Findings from the free comments and open questions were not formally analysed as a part of the present work.

Summary box

Section 1: What is already known on this topic

The very high acquisition costs of biologic TNF inhibitors such as Humira have resulted in restricted access across global healthcare economies.

In 2018, NHS England published their intentions with instructions that at least 80% of patients who use Humira should be switched to the best value biosimilar within 12 months.

The patient organisations welcomed NHS's policy, but they required that patients should be fully informed about the treatment options and health professionals adopt the principles of shared decision-making.

Section 2: What this study adds

Participants who responded to the survey request by the patient organisations reported poor satisfaction with the switching process to biosimilar due to paucity of information and training.

Where good information and training were provided, it was associated with reduction in self-reported side effects and injection related pain as well as greater ease of use of the injection device and management and control of symptoms.

Authors Contributions: PCT assumes overall responsibility for the work and all the reported data. CJ, AB, SD, SB, HA designed the patient survey and were involved in data collection. PCT and KK wrote the first draft of the manuscript. KK, DP-A and PCT analysed the data. All authors contributed to discussion and interpretation of the results, critically reviewed the manuscript and approved the final version to be submitted.

Transparency: PCT affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; there have been no discrepancies from the study as planned

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Ethical approval: This was an anonymized, self-administered, web-based survey for the purposes of service evaluation among patients who provided electronic consent of

voluntary participation.

Data sharing: Raw anonymous data is available to researchers on application to the patient organisations involved who will jointly assess any applications.

Dissemination Statement: The results will be shared with the study participants and the contributing patient organisations.

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Figure legends.

Figure 1.

Donut charts illustrating the percentage of patients expressing different levels of satisfaction with various experiences associated with the switching process.

Figure 2.

Adjusted odds rations illustrating the influence of training and information from healthcare professionals in improving perception of the new biosimilar. Adjusted odds ratio and 95% confidential intervals were calculated by a multiple categorical logistic regression analysis using gender, self-reported disease activity and biosimilar brands as adjusted variables. Data to the left of the adjusted odds ratio of 1 indicates a more favourable perception.

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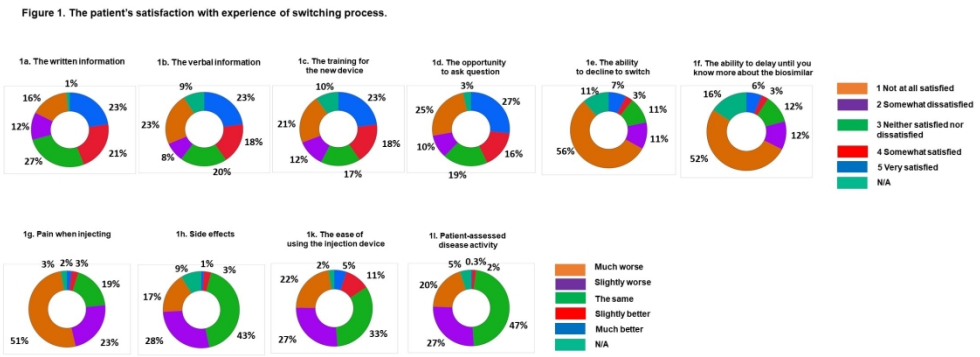

Figure 1. Donut charts illustrating the percentage of patients expressing different levels of satisfaction with various experiences associated with the switching process.

602x338mm (96 x 96 DPI)

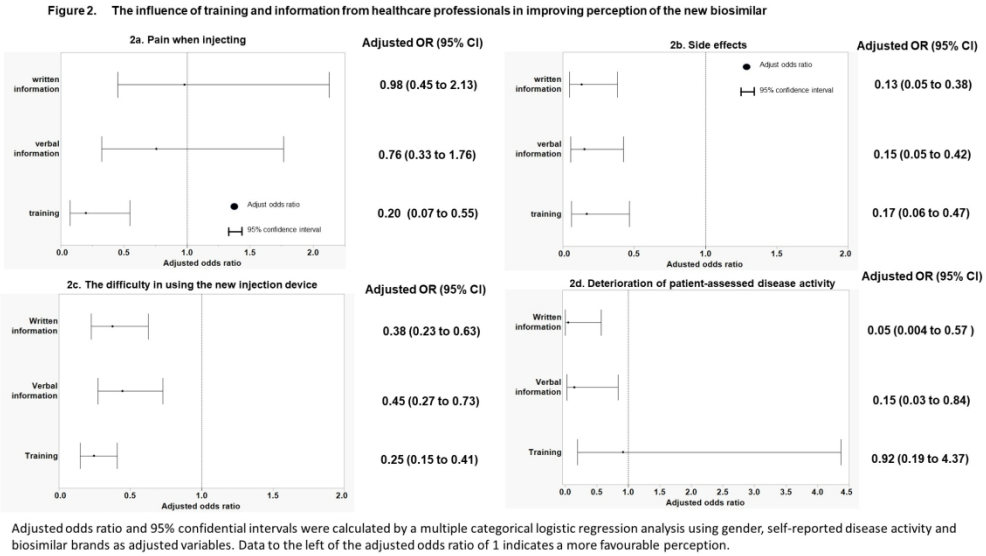

Figure 2. Adjusted odds rations illustrating the influence of training and information from healthcare professionals in improving perception of the new biosimilar. Adjusted odds ratio and 95% confidential intervals were calculated by a multiple categorical logistic regression analysis using gender, self-reported disease activity and biosimilar brands as adjusted variables. Data to the left of the adjusted odds ratio of 1 indicates a more favourable perception.

602x338mm (96 x 96 DPI)

We want to understand the recent experiences of people living in the UK who have switched from Humira to an adalimumab biosimilar medication.

If you haven't been asked to switch yet please note that we will keep this survey open for a few months so do feel that you can come back to it.

This survey is for only for people living in the UK aged 18+

1. Do you live in the UK?

- ○ Yes
- ○ No

2. What area of the UK do you live in?

- ○ Scotland
- ○ Wales
- ○ Northern Ireland
- ○ Isle of Man
- ○ Channel Islands
- ○ North East and Yorkshire
- ○ North West
- ○ Midlands
- ○ East of England
- ○ South West
- ○ South East
- ○ London

3. Were you being treated with Humira (adalimumab) during 2018?

- ○ Yes
- ○ No

4. What medical condition was your Humira primarily prescribed for?

- ○ Axial spondyloarthritis including ankylosing spondylitis (AS)
- ○ Crohn's Disease
- ○ Ulcerative colitis
- ○ Another form of IBD
- ○ Hidradenitis Suppurativa
- ○ Psoriasis
- ○ Psoriatic arthritis
- ○ Rheumatoid arthritis (RA)
- ○ Juvenile Idiopathic Arthritis (JIA)
- ○ Uveitis
- ○ Other (please specify)

5. Have you switched from Humira to an adalimumab biosimilar?

- ○ Yes
- ○ No

6. Did your consultant, specialist nurse or pharmacist seek your consent to switch from Humira to a biosimilar?

- ○ Yes
- ○ No
- ○ Not sure / can't remember

7. Which biosimilar medication have you switched to?

- ○ Amgevita
- ○ Hulio
- ○ Hyrimoz
- ○ Imraldi
- ○ Don't know/not sure

8. How long were you taking Humira prior to being switched?

- ○ 3 months or less
- ○ More than 3 months to 1 year
- ○ More than 1 year to 5 years
- ○ More than 5 years to 10 years
- ○ More than 10 years

9. Thinking about the time you were being treated with Humira (adalimumab) how well do you feel your disease was controlled? Please use the scale of 1 to 5 where 1 means your condition was not controlled well at all and 5 means very well controlled

Not at all satisfied	Somewhat dissatisfied	Neither satisfied nor dissatisfied	Somewhat satisfied	Very satisfied	N/A
○	○	○	○	○	○

Now, thinking about the process of switching

10. In which of the following ways did you first hear you may be asked to switch to a biosimilar?

- ○ I was told about the potential to switch face to face in clinic by my consultant
- ○ I was told about the potential to switch face to face in clinic by my specialist nurse
- ○ I was invited to a patient information meeting about biosimilars
- ○ I received a letter from the hospital
- ○ I received a letter from the homecare delivery company
- ○ I received a telephone call from the specialist nurse
- ○ I received a telephone call from the homecare delivery company
- ○ I received a telephone call from the hospital pharmacy
- ○ I received no prior notice of my treatment being switched
- ○ Other (please specify)

11. Thinking about what you heard about switching, which of the following information did you pick up from what you were told or given in writing?

- ○ Switching to biosimilars will save the NHS money
- ○ Biosimilars are almost identical and I should notice no difference in my symptoms or side effects
- ○ Switching to biosimilars will mean my hospital department would benefit and might be able to offer improved services to patients
- ○ Switching to biosimilars means more patients would be able to get prescribed these medications
- ○ I had a choice and could choose not to switch if I preferred
- ○ I would be switched to a biosimilar medication and there were no other options
- ○ I was given links to more information on biosimilars (e.g. on patient organisation websites)
- ○ Who to contact with any queries I may have about biosimilars
- ○ Other (please specify)

12. Thinking about your experience of the switching process, how would you rate your satisfaction with...

	Not at all satisfied	Somewhat dissatisfied	Neither satisfied nor dissatisfied	Somewhat satisfied	Very satisfied	N/A
The written information you received about the switch to a biosimilar	○	○	○	○	○	○
The verbal information you received about the switch from your healthcare professional	○	○	○	○	○	○
The opportunity to ask questions	○	○	○	○	○	○
The training for the new device	○	○	○	○	○	○
The ability to decline to switch	○	○	○	○	○	○
The ability to delay switching until you knew more about the biosimilar	○	○	○	○	○	○

13. What, if anything, do you think could have been done better to help the switching process run more smoothly?

Now, thinking about the biosimilar you were switched to

14. How many injections of the new biosimilar would you estimate you have taken so far?

- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 7
- ○ 8
- ○ 9
- ○ 10
- ○ More than 10

15. Thinking about how you feel the new biosimilar is working for you in terms of managing your symptoms compared with Humira would you say it is...

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

16. And what about in terms of side effects?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

17. And pain when injecting?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

18. And the ease of using the injection device?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

19. And the ease of accessing the injection device via the external packaging?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

20. And the Homecare company arrangements?

Much worse	Slightly worse	The same	Slightly better	Much better	N/A
○	○	○	○	○	○

21. And overall, how satisfied are you with your new biosimilar? Scale of 1 to 5 where 5 is very satisfied and 1 is not at all satisfied

Not at all satisfied	Somewhat satisfied	Neither	Satisfied	Very satisfied
○	○	○	○	○

And why do you say that?

22. And have you shared any concerns you may have with your consultant, specialist nurse, pharmacist, physiotherapist or GP?

○ Yes
○ No
○ I didn't know I could

23. And do you feel they have they offered you a satisfactory solution?

○ Yes, I was offered a switch back to my original treatment
○ Yes, I was offered a switch to another treatment
○ No
○ Other (please specify)

24. What do you think is most important for hospitals to be aware of as part of the switching process for new patients going forward?

25. Do you have any other comments about your experience of the biosimilar switching process?

Thank you for your time, can we just ask you for some information about yourself.

26. Gender

- ○ Female
- ○ Male
- ○ Other
- ○ Prefer not to say

27. Age

- ○ 18-24
- ○ 25-34
- ○ 35-44
- ○ 45-54
- ○ 55-64
- ○ 65+
- ○ Prefer not to say

If you are experiencing side effects with any medication please do remember anyone can report suspected side effects using the Yellow Card Scheme. Visit: mhra.gov.uk/yellowcard or call 0808 100 3352 for a paper form.

Do also speak to your rheumatologist or rheumatology nurse.

TableS1. Comparison of characteristics of the participants between satisfied group and dissatisfied group with each experience in switching process.

Characteristics	The written information					The verbal information					The training for the new device				
	Satisfied group (N=394)		Dissatisfied group (N=249)		*p value*	Satisfied group (N=362)		Dissatisfied group (N=277)		*p value*	Satisfied group (N=364)		Dissatisfied group (N=295)		*p value*
Gender, n (%)					0.5201					0.3189					**0.00458***
Female	258	(66)	170	(69)		235	(65)	192	(70)		235	(65)	214	(74)	
Male	130	(33)	75	(30)		121	(34)	82	(30)		125	(34)	74	(26)	
Prefer not to say	4	(1)	1	(0)		4	(1)	1	(0)		3	(1)	2	(1)	
Age, n (%)					0.0546					**0.0003***					0.1091
18-24	28	(7)	24	(10)		25	(7)	27	(10)		26	(7)	26	(9)	
25-34	56	(14)	52	(21)		51	(14)	61	(22)		57	(16)	65	(22)	
35-44	70	(18)	50	(20)		55	(15)	59	(21)		71	(20)	62	(21)	
45-54	94	(24)	58	(23)		85	(23)	66	(24)		74	(20)	61	(21)	
55-64	80	(20)	40	(16)		78	(22)	38	(14)		77	(21)	45	(15)	
65+	61	(15)	24	(10)		63	(17)	25	(9)		54	(15)	35	(12)	
Prefer not to say	5	(1)	1	(0)		5	(1)	1	(0)		5	(1)	1	(0)	
Living areas, n (%)					0.3173					**0.0267***					0.9099
South East	101	(26)	69	(28)		96	(27)	72	(26)		95	(26)	80	(27)	
South West	75	(19)	43	(17)		76	(21)	48	(17)		68	(19)	60	(20)	
North East and Yorkshire	52	(13)	27	(11)		53	(15)	28	(10)		49	(13)	34	(12)	
Midlands	42	(11)	41	(16)		31	(9)	51	(18)		46	(13)	33	(11)	
East of England	46	(12)	17	(7)		37	(10)	28	(10)		39	(11)	28	(9)	
North West	31	(8)	17	(7)		26	(7)	18	(7)		28	(8)	19	(6)	
London	22	(6)	20	(8)		19	(5)	22	(8)		21	(6)	24	(8)	
Scotland	16	(4)	6	(2)		14	(4)	4	(1)		8	(2)	11	(4)	
Wales	6	(2)	6	(2)		7	(2)	4	(1)		6	(2)	4	(1)	

Northern Ireland	1	(0)	1	(0)		1	(0)	1	(0)		2	(1)	1	(0)	
Channel Islands	1	(0)	1	(0)		1	(0)	0	(0)		1	(0)	0	(0)	
Isle of Wight	1	(0)	1	(0)		1	(0)	1	(0)		1	(0)	1	(0)	
Medical conditions, n (%)					0.2988					0.0587					0.1358
CD	144	(37)	74	(30)		122	(34)	93	(34)		125	(35)	104	(35)	
RA/JIA	104	(27)	64	(26)		106	(29)	54	(19)		94	(26)	69	(23)	
AS	79	(20)	53	(21)		70	(19)	60	(22)		82	(23)	49	(17)	
PsA	22	(6)	24	(10)		23	(6)	30	(11)		22	(6)	30	(10)	
UC	25	(6)	19	(8)		23	(6)	26	(9)		21	(6)	24	(8)	
Psoriasis	15	(4)	11	(4)		13	(4)	11	(4)		14	(4)	12	(4)	
Others	3	(1)	4	(2)		4	(1)	3	(1)		4	(1)	7	(2)	
Period of Humira use before switching, n (%)					0.1228					**0.0095***					0.3304
3 months or less	14	(4)	14	(6)		12	(3)	11	(4)		14	(4)	16	(5)	
More than 3 months to 1 year	66	(17)	51	(20)		60	(17)	53	(19)		61	(17)	58	(20)	
More than 1 year to 5 years	208	(53)	130	(52)		177	(49)	159	(57)		188	(52)	152	(52)	
More than 5 years to 10 years	68	(17)	42	(17)		72	(20)	41	(15)		68	(19)	53	(18)	
More than 10 years	38	(10)	12	(5)		41	(11)	13	(5)		33	(9)	16	(5)	
Self-reported disease activity, n (%)					**0.0282***					**0.041***					**0.0358***
Very well controlled	243	(62)	157	(63)		229	(63)	174	(63)		226	(62)	190	(65)	
controlled well	104	(26)	64	(26)		99	(27)	69	(25)		84	(23)	80	(27)	
Neither	40	(10)	21	(8)		26	(7)	25	(9)		42	(12)	18	(6)	
Not controlled	1	(0)	6	(2)		2	(1)	7	(3)		4	(1)	5	(2)	
Not controlled well at all	6	(2)	0	(0)		6	(2)	0	(0)		7	(2)	1	(0)	

No. of injections of the new biosimilar before survey, n (%)					0.3279					0.4633				0.1015
1	35	(9)	27	(11)		32	(9)	29	(11)		37	(10)	31	(11)	
2	54	(14)	26	(11)		43	(12)	31	(11)		51	(14)	25	(9)	
3	55	(14)	25	(10)		49	(14)	28	(10)		48	(13)	31	(11)	
4	37	(9)	31	(13)		40	(11)	29	(11)		40	(11)	35	(12)	
5	25	(6)	26	(11)		22	(6)	21	(8)		16	(4)	30	(10)	
6	60	(15)	30	(12)		52	(14)	46	(17)		50	(14)	46	(16)	
7	18	(5)	12	(5)		15	(4)	13	(5)		13	(4)	11	(4)	
8	33	(8)	22	(9)		22	(6)	27	(10)		26	(7)	27	(9)	
9	10	(3)	8	(3)		12	(3)	9	(3)		9	(2)	8	(3)	
10	13	(3)	12	(5)		18	(5)	12	(4)		19	(5)	11	(4)	
More than 10	52	(13)	27	(11)		55	(15)	27	(10)		53	(15)	36	(12)	

CD, Crohn's Disease, RA, Rheumatoid arthritis, JIA, Juvenile Idiopathic Arthritis, AS, Axial spondyloarthritis including ankylosing spondylitis, PsA, Psoriatic arthritis, UC, Ulcerative colitis, Valuables presented as n (%), P values were assigned based on the chi-square test for categorical value when it's expected value is higher than 10 and Fisher's exact test was conducted if the expected values of categorical values were smaller than 10. *P values less than 0.05 was considered statistically significant.

Table S2a

		Comparison of proportion of patients with "worse perception" or "better perception" on the new biosimilars between those expressing satisfaction and dissatisfaction in the switching process									
		The written information									
		satisfied group (N=394)		dissatisfied group (N=249)		Neither (N=238)		N/A (N=13)		*unadjusted OR (95%CI)	*p value
Side effects	worse perception, n (%)	118	(30)	158	(63)	117	(49)	7	(54)	**0.15 (0.06-0.40)**	**<.0001†**
	better perception, n (%)	25	(6)	5	(2)	6	(3)	1	(8)		
	the same, n (%)	218	(56)	58	(23)	101	(42)	1	(8)		
	N/A, n (%)	31	(8)	28	(11)	14	(6)	4	(31)		
Pain when injecting	worse perception, n (%)	275	(70)	194	(78)	183	(77)	9	(69)	0.90 (0.45-1.81)	0.861
	better perception, n (%)	22	(6)	14	(6)	6	(3)	0	(0)		
	the same, n (%)	87	(22)	31	(13)	46	(19)	1	(8)		
	N/A, n (%)	8	(2)	9	(4)	3	(1)	3	(23)		
The ease of using the injection device	worse perception, n (%)	159	(40)	153	(62)	118	(50)	5	(38)	**0.35 (0.21-0.58)**	**<.0001†**
	better perception, n (%)	77	(20)	26	(10)	35	(15)	2	(15)		
	the same, n (%)	146	(37)	64	(26)	81	(34)	3	(23)		
	N/A, n (%)	11	(3)	5	(2)	3	(1)	3	(23)		
Managing symptoms	worse perception, n (%)	112	(28)	172	(69.1)	123	(52)	5	(38)	**0.11 (0.02-0.49)**	**0.0011†**
	better perception, n (%)	12	(3)	2	(0.8)	4	(2)	0	(0)		
	the same, n (%)	254	(64)	57	(22.9)	103	(44)	5	(38)		
	N/A, n (%)	16	(4)	18	(7.23)	6	(3)	3	(23)		

Valuables presented as n (%). *Comparison of frequency of responses with "worse perception" and "better perception" of the new biosimilar compared to originator between "satisfied group" and "dissatisfied group" with the experiences in the switching process to biosimilar were expressed as unadjusted odds ratios (OR), 95% confidential intervals (95%CI) and *p* values. Responses expressing "3 (neither)" or "not applicable (N/A)" in terms of satisfaction with the services in switching process and "the same" or "N/A" in terms of

the perception of the new biosimilar were excluded from the analysis. P values were assigned based on the chi-square test for categorical value when it's expected value is higher than 10 and Fisher's exact test was conducted if the expected values of categorical values were smaller than 10. †P values less than 0.05 was considered statistically significant.

Table S2b **Comparison of proportion of patients with "worse perception" or "better perception" on the new biosimilars between those expressing satisfaction and dissatisfaction in the switching process**

		The verbal information									
		Satisfied group (N=362)		Dissatisfied group (N=277)		Neither (N=175)		N/A (N=79)		*unadjusted OR (95%CI)	*p value
Side effects	Worse perception, n (%)	117	(33)	164	(59)	83	(47)	34	(43)	**0.15 (0.06-0.40)**	**<.0001†**
	Better perception, n (%)	24	(7)	5	(2)	5	(3)	3	(4)		
	The same, n (%)	192	(53)	79	(29)	76	(43)	31	(39)		
	N/A, n (%)	27	(8)	29	(10)	11	(6)	11	(14)		
Pain when injecting	Worse perception, n (%)	258	(71)	225	(82)	125	(72)	52	(66)	0.67 (0.30-1.50)	0.428
	Better perception, n (%)	17	(5)	10	(4)	13	(7)	3	(4)		
	The same, n (%)	76	(21)	34	(12)	34	(20)	20	(25)		
	N/A, n (%)	10	(3)	7	(3)	2	(1)	4	(5)		
The ease of using the injection device	Worse perception, n (%)	153	(42)	166	(60)	84	(48)	32	(41)	**0.45 (0.28-0.72)**	**0.0008†**
	Better perception, n (%)	66	(18)	32	(12)	26	(15)	16	(20)		
	The same, n (%)	130	(36)	73	(27)	63	(36)	27	(34)		
	N/A, n (%)	12	(3)	4	(1)	2	(1)	4	(5)		
Managing symptoms	Worse perception, n (%)	117	(32)	175	(63)	89	(51)	32	(41)	**0.20 (0.05-0.74)**	**0.0177†**
	Better perception, n (%)	10	(3)	3	(1)	(3)	(2)	2	(3)		
	The same, n (%)	221	(61)	76	(27)	(75)	(43)	45	(57)		
	N/A, n (%)	13	(4)	23	(8)	(7)	(4)	0	(0)		

Valuables presented as n (%). *Comparison of frequency of responses with "worse perception" and "better perception" of the new biosimilar compared to originator between “satisfied group” and “dissatisfied group” with the experiences in the switching process to biosimilar were expressed as unadjusted odds ratios (OR), 95% confidential intervals (95%CI) and *p* values. Responses expressing “3 (neither)” or “not applicable (N/A)“ in terms of satisfaction with the services in switching process and “the same” or “N/A” in terms of the perception of the new biosimilar were excluded from the analysis. P values were assigned based on the chi-square test for categorical value when it’s expected value is higher than 10 and Fisher’s exact test was conducted if the expected values of categorical values were smaller than 10. †P values less than 0.05 was considered statistically significant.

Table S2c

Comparison of proportion of patients with "worse perception" or "better perception" on the new biosimilars between those expressing satisfaction and dissatisfaction in the switching process

		The training									
		satisfied group (N=364)		dissatisfied group (N=295)		Neither (N=149)		N/A (N=86)		*unadjusted OR (95%CI)	*p value
Side effects	worse perception, n (%)	133	(37)	176	(60)	65	(44)	25	(29)	**0.15 (0.06-0.41)**	**<.0001†**
	better perception, n (%)	25	(7)	5	(2)	4	(3)	3	(4)		
	the same, n (%)	176	(48)	90	(31)	65	(44)	47	(55)		
	N/A, n (%)	29	(8)	24	(8)	15	(10)	10	(12)		
The ease of Pain when injecting	worse perception, n (%)	254	(70)	242	(83)	113	(76)	52	(60)	**0.19 (0.07-0.49)**	**0.0001†**
	better perception, n (%)	28	(8)	5	(2)	8	(5)	2	(2)		
	the same, n (%)	75	(21)	38	(13)	27	(18)	24	(28)		
	N/A, n (%)	6	(2)	8	(3)	1	(1)	8	(9)		
The ease of using the injection device	worse perception, n (%)	134	(37)	194	(66)	76	(51)	32	(37)	**0.24 (0.15-0.40)**	**<.0001†**
	better perception, n (%)	79	(22)	28	(10)	20	(14)	13	(15)		
	the same, n (%)	144	(40)	66	(22)	51	(34)	32	(37)		
	N/A, n (%)	6	(2)	6	(2)	1	(1)	9	(10)		
The ease of Managing symptoms	worse perception, n (%)	136	(37)	178	(60)	67	(45)	33	(38)	0.38 (0.11-1.30)	0.1412
	better perception, n (%)	8	(2)	4	(1)	4	(3)	2	(2)		
	the same, n (%)	201	(55)	97	(33)	73	(49)	46	(53)		
	N/A, n (%)	18	(5)	16	(5)	4	(3)	5	(6)		

Valuables presented as n (%). *Comparison of frequency of responses with "worse perception" and "better perception" of the new biosimilar compared to originator between "satisfied group" and "dissatisfied group" with the experiences in the switching process to biosimilar were expressed as unadjusted odds ratios (OR), 95% confidential intervals (95%CI) and *p* values. Responses expressing "3 (neither)" or "not applicable (N/A)" in terms of satisfaction with the services in switching process and "the same" or "N/A" in terms of the perception of the new biosimilar were excluded from the analysis. P values were assigned based on the chi-square test for categorical value when it's expected value is higher than 10 and Fisher's exact test was conducted if the expected values of categorical values were smaller than 10. †P values less than 0.05 was considered statistically significant.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P.4 line5
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P.4 line12 to P.5 line11
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P.7 line2 to P.9 line7
Objectives	3	State specific objectives, including any prespecified hypotheses	P.9 line11 to 13
Methods			
Study design	4	Present key elements of study design early in the paper	P.9 line16 to 17
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P.10 line1 to 12, and P.10 line16 to P.11 line5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P.10 line 13 to 16, and P.12 line16 to P.13 line4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P.11 line18 to P.12 line17
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P.11 line 6 to 17
Bias	9	Describe any efforts to address potential sources of bias	Not applicable because this was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations.
Study size	10	Explain how the study size was arrived at	Not applicable because this was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Not applicable because we did not handle with quantitative variables.

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P. 13 line6 to 18
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable because we did not examine subgroups and interactions
		(*c*) Explain how missing data were addressed	Not described.
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	Not applicable because this was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations.
		(*e*) Describe any sensitivity analyses	Not applicable because we did not conduct any sensitivity analyses
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P.14 line3 to 4
		(b) Give reasons for non-participation at each stage	Not applicable because this was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations.
		(c) Consider use of a flow diagram	Not applicable because this was an anonymized, self-administered, web-based survey among patients who interacted with the following patient organisations.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P.14 line 4 to 10
		(b) Indicate number of participants with missing data for each variable of interest	Described in Table 1 and 2.
Outcome data	15*	Report numbers of outcome events or summary measures	Not applicable because all participants experienced the switching process.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	P.15 line18 to P.17 line10
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable because continuous variables were not analysed

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable because we did not evaluate the relative risk
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable because we did not conduct analysis of subgroup and interactions, and sensitivity analyses
Discussion			
Key results	18	Summarise key results with reference to study objectives	P.17 line16 to p.18 line5
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P.19 line16 to P.20 line3
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P.20 line4 to P.21 line5
Generalisability	21	Discuss the generalisability (external validity) of the study results	p.21 line6 to 16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p.25 line 10 to 11

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.